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=> s lr3 or lr3a or lrp5 or lrp7 or (ldl (w) receptor-related (w) protein (w) 5)
5 FILES SEARCHED...
L1 980 LR3 OR LR3A OR LRP5 OR LRP7 OR (LDL (W) RECEPTOR-RELATED (W)
PROTEIN (W) 5)

=> s endothelial (w) cells or osteoblasts
L2 308766 ENDOTHELIAL (W) CELLS OR OSTEOBLASTS

=> s wnt (w) protein or dkk (w) protein
4 FILES SEARCHED...
L3 4961 WNT (W) PROTEIN OR DKK (W) PROTEIN

=> s l1 and l2
L4 74 L1 AND L2

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, BIOTECHNO, USPATFULL'
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L5 ANSWER 1 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2005:36968 USPATFULL
TITLE: Microorganisms for therapy
INVENTOR(S): Szalay, Aladar A., Highland, CA, UNITED STATES
Timiryasova, Tatyana, San Diego, CA, UNITED STATES
Yu, Yong A., San Diego, CA, UNITED STATES
Zhang, Qian, San Diego, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005031643	A1	20050210
APPLICATION INFO.:	US 2004-872156	A1	20040618 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2003-13826	20030618
	EP 2003-18478	20030814
	EP 2003-24283	20031022

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON, PC, 12390 EL CAMINO REAL, SAN DIEGO, CA, 92130-2081
NUMBER OF CLAIMS: 86
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 11773
AB Therapeutic methods and microorganisms therefore are provided. The
microorganisms are designed to accumulate in immunoprivileged tissues
and cells, such as in tumors and other proliferating tissue and in
inflamed tissues, compared to other tissues, cells and organs, so that
they exhibit relatively low toxicity to host organisms. The
microorganisms also are designed or modified to result in leaky cell
membranes of cells in which they accumulate, resulting in production of

antibodies reactive against proteins and other cellular products and
also permitting exploitation of proliferating tissues, particularly
tumors, to produce selected proteins and other products. Methods for
making tumor specific antibodies and also methods of making gene
products encoded by the microorganism as well as antibodies reactive
therewith are provided.

=> d l5 1- ibib,abs
YOU HAVE REQUESTED DATA FROM 45 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2005:36968 USPATFULL
TITLE: Microorganisms for therapy
INVENTOR(S): Szalay, Aladar A., Highland, CA, UNITED STATES
Timiryasova, Tatyana, San Diego, CA, UNITED STATES
Yu, Yong A., San Diego, CA, UNITED STATES
Zhang, Qian, San Diego, CA, UNITED STATES

	NUMBER	KIND	DATE
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DOCUMENT TYPE: Utility
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NUMBER OF CLAIMS: 86
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NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 11773
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they exhibit relatively low toxicity to host organisms. The
microorganisms also are designed or modified to result in leaky cell
membranes of cells in which they accumulate, resulting in production of
antibodies reactive against proteins and other cellular products and
also permitting exploitation of proliferating tissues, particularly
tumors, to produce selected proteins and other products. Methods for
making tumor specific antibodies and also methods of making gene
products encoded by the microorganism as well as antibodies reactive
therewith are provided.

L5 ANSWER 2 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:320589 USPATFULL
TITLE: Rationally designed antibodies
INVENTOR(S): Bowdish, Katherine S., Del Mar, CA, UNITED STATES
Frederickson, Shana, Solana Beach, CA, UNITED STATES
Renshaw, Mark, Solana Beach, CA, UNITED STATES
Orencia, Cecelia, Del Mar, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004253242	A1	20041216
APPLICATION INFO.:	US 2003-737290	A1	20031215 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-452590, filed
on 2 Jun 2003, PENDING Continuation-in-part of Ser. No.
US 2002-307724, filed on 2 Dec 2002, PENDING
Continuation-in-part of Ser. No. US 2001-6593, filed on
5 Dec 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-251448P	20001205 (60)
	US 2001-288889P	20010504 (60)
	US 2001-294068P	20010529 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Mark Farber, C/O, Alexion Pharmaceuticals, Inc., 352
Knotter Drive, Cheshire, CT, 06410
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 59 Drawing Page(s)
LINE COUNT: 5086
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antibodies or fragments thereof having CDR regions replaced or fused
with biologically active peptides are described. Flanking sequences may
optionally be attached at one or both the carboxy-terminal and
amino-terminal ends of the peptide in covalent association with adjacent
framework regions. Compositions containing such antibodies or fragments
thereof are useful in therapeutic and diagnostic modalities.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 45 USPATFULL on STN

ACCESSION NUMBER: 2004:309387 USPATFULL
TITLE: Transgenic animal model of bone mass modulation
INVENTOR(S): Askew, G. Roger, Boxford, MA, UNITED STATES
Babij, Philip, Dunstable, MA, UNITED STATES
Bex, Frederick James, III, Newtown Square, PA, UNITED STATES
Nest Bodine, Peter Van, Havertown, PA, UNITED STATES
PATENT ASSIGNEE(S): Wyeth, Madison, NJ, UNITED STATES, 07940 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004244069	A1	20041202
APPLICATION INFO.:	US 2003-680287	A1	20031008 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2002-US14876, filed on 13 May 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-290071P	20010511 (60)
	US 2001-291311P	20010517 (60)
	US 2002-353058P	20020201 (60)
	US 2002-361293P	20020304 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 44
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 61 Drawing Page(s)
LINE COUNT: 8213
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to express the HBM protein in animal cells and transgenic animals. The present invention also relates to transgenic animals expressing the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The invention provides nucleic acids, including coding sequences, oligonucleotide primers and probes, proteins, cloning vectors, expression vectors, transformed hosts, methods of developing pharmaceutical compositions, methods of identifying molecules involved in bone development, and methods of diagnosing and treating diseases involved in bone development. In preferred embodiments, the present invention is directed to methods for treating, diagnosing and preventing osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:299859 USPATFULL
TITLE: Compositions and methods for treating osteoporosis
INVENTOR(S): Stoch, Selwyn Aubrey, Clark, NJ, UNITED STATES
Orloff, John, Princeton Junction, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004235728	A1	20041125
APPLICATION INFO.:	US 2004-494542	A1	20040430 (10)
	WO 2002-US35341		20021104

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-337785P	20011108 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 1427
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to pharmaceutical compositions comprising a cathepsin K inhibitor which are useful for treating such conditions as bone resorption, osteoporosis, arthritis, tumor metastases, Paget's disease, and other metabolic bone disorders characterized by increased bone resorption.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:282022 USPATFULL
TITLE: Transgenic animal model of bone mass modulation
INVENTOR(S): Babij, Philip, Newbury Park, CA, UNITED STATES
Bex, Frederick James, Newton Square, PA, UNITED STATES
Bodine, Peter Van Nest, Havertown, PA, UNITED STATES
Askew, G. Roger, Boxford, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004221326	A1	20041104
APPLICATION INFO.:	US 2004-477238	A1	20040412 (10)
	WO 2002-US14876		20020513

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-60290071	20010511
	US 2001-60291311	20010517
	US 2002-60353058	20020201

US 2002-60361293 20020304
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 61 Drawing Page(s)
LINE COUNT: 7878
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to express the HBM protein in animal cells and transgenic animals. The present invention also relates to transgenic animals expressing the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The invention provides nucleic acids, including coding sequences, oligonucleotide primers and probes, proteins, cloning vectors, expression vectors, transformed hosts, methods of developing pharmaceutical compositions, methods of identifying molecules involved in bone development, and methods of diagnosing and treating diseases involved in bone development. In preferred embodiments, the present invention is directed to methods for treating, diagnosing and preventing osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:275671 USPATFULL
TITLE: Compositions and methods for characterizing and regulating Wnt pathways
INVENTOR(S): MacDougald, Ormond A., Ypsilanti, MI, UNITED STATES
Longo, Kenneth A., Ann Arbor, MI, UNITED STATES
Ross, Sarah E., Cambridge, MA, UNITED STATES
PATENT ASSIGNEE(S): The Regents of the University of Michigan, Ann Arbor, MI (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004216176	A1	20041028
APPLICATION INFO.:	US 2004-755594	A1	20040112 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-439386P	20030110 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Tanya A. Arenson, MEDLEN & CARROLL, LLP, Suite 350, 101 Howard Street, San Francisco, CA, 94105
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 1162
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to transgenic animal models for altered Wnt expression. The present invention also provides methods for generating animal models and screening methods for identifying biologically active compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 7 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:228196 USPATFULL
TITLE: High bone mass gene of 11q13.3
INVENTOR(S): Carulli, John P., Southboro, MA, UNITED STATES
Little, Randall D., Newtonville, MA, UNITED STATES
Recker, Robert R., Omaha, NE, UNITED STATES
Johnson, Mark L., Omaha, NE, UNITED STATES
PATENT ASSIGNEE(S): Genome Therapeutics Corporation, Waltham, MA, UNITED STATES (U.S. corporation)
Creighton University, Omaha, NE, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004176582	A1	20040909
APPLICATION INFO.:	US 2003-731739	A1	20031210 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-544398, filed on 5 Apr 2000, PENDING Continuation-in-part of Ser. No. US 1999-229319, filed on 13 Jan 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-71449P	19980113 (60)
	US 1998-105511P	19981023 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 74
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Page(s)
LINE COUNT: 12994
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to isolate and detect a high bone mass gene and a corresponding wild-type gene, and mutants thereof. The present invention also relates to the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The

genes identified in the present invention are implicated in bone
development. The invention also provides nucleic acids, including coding
sequences, oligonucleotide primers and probes, proteins, cloning
vectors, expression vectors, transformed hosts, methods of developing
pharmaceutical compositions, methods of identifying molecules involved
in bone development, and methods of diagnosing and treating diseases
involved in bone development. In preferred embodiments, the present
invention is directed to methods for treating, diagnosing and preventing
osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:197578
USPATFULL
TITLE: Lp mammalian proteins; related reagents
INVENTOR(S): Amegadzie, Bernard Yaovi, Malvern, PA, UNITED STATES
Basinski, Margaret Barbara, Indianapolis, IN, UNITED
STATES
Scott, William L., Indianapolis, IN, UNITED STATES LR
Chen, Dayue, Carmel, IN, UNITED STATES
Huang, Chongxi, Indianapolis, IN, UNITED STATES
Keleher, Gerald Patrick, Indianapolis, IN, UNITED
STATES
Perkins, Douglas Raymond, New Palestine, IN, UNITED
STATES
Rosteck, Paul Robert, Indianapolis, IN, UNITED STATES
Rowlinson, Scott William, Indianapolis, IN, UNITED
STATES
Sankhavaram, Patanjali Raghavac, Carmel, IN, UNITED
STATES
Seno, Eugene Thomas, Weybridge, VT, UNITED STATES
Su, Eric Wen, Carmel, IN, UNITED STATES
Zhi, Yu, Indianapolis, IN, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004152885	A1	20040805
APPLICATION INFO.:	US 2003-480172	A1	20030827 (10)
	WO 2002-US5093		20020301

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gerald P keleher, Eli Lilly & Company, Patent Division,
PO Box 6288, Indianapolis, IN, 46206-6288
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 12032
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Isolated nucleic acid molecules encoding polypeptides from a human,
reagents related thereto (including purified polypeptides specific
antibodies) are provided. Methods of using said reagents and diagnostic
kits are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 9 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:197345
USPATFULL
TITLE: Regulation of transcription elongation factors
INVENTOR(S): Rana, Tariq M., Shrewsbury, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004152651	A1	20040805
APPLICATION INFO.:	US 2003-635854	A1	20030805 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-423198P	20021101 (60)
	US 2003-439301P	20030109 (60)
	US 2002-433097P	20021213 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 87
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 40 Drawing Page(s)
LINE COUNT: 5412
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to agents, including siRNA and shRNA
molecules, small molecules, antisense strands, and ribozymes that are
targeted to transcription elongation factors (TEFs), including CDK9 and
CycT1, subunits of P-TEFb, Spt4 and Spt5, subunits of DSIF (DRB
Sensitivity-Inducing Factor (DSIF)), and Spt6. The present invention
also relates to methods for treating disorders associated with aberrant
or unwanted TEF expression or activity, including HIV and disorders
characterized by unwanted or aberrant cellular proliferation or
differentiation, such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 10 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:196424
USPATFULL
TITLE: Lectin compositions and methods for modulating an

immune response to an antigen
INVENTOR(S): Segal, Andrew H., Boston, MA, UNITED STATES
Young, Elihu, Sharon, MA, UNITED STATES
PATENT ASSIGNEE(S): Genitrix, LLC (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004151728	A1	20040805
APPLICATION INFO.:	US 2003-666834	A1	20030919 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-404823P	20020820 (60)
	US 2003-487407P	20030715 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE, BOSTON, MA, 02199
NUMBER OF CLAIMS: 77
EXEMPLARY CLAIM: 1
LINE COUNT: 39129
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 11 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:178323 USPATFULL
TITLE: Molecular determinants of myeloma bone disease and uses thereof
INVENTOR(S): Shaughnessy, John D., Little Rock, AR, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004137489	A1	20040715
APPLICATION INFO.:	US 2003-727461	A1	20031204 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-431040P	20021205 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 43 Drawing Page(s)
LINE COUNT: 1105
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB To identify molecular determinants of lytic bone disease in multiple myeloma, the expression profiles of .about.12,000 genes in CD138-enriched plasma cells from newly diagnosed multiple myeloma patients exhibiting no radiological evidence of lytic lesions (n=28) were compared to those with .gtoreq.3 lytic lesions (n=47). Two secreted WNT signaling antagonists, soluble frizzled related protein 3 (SFRP-3/FRZB) and the human homologue of Dickkopf-1 (DKK1), were expressed in 40 of 47 with lytic bone lesions, but only 16 of 28 lacking bone lesions (P<0.05). DKK1 and FRZB were not expressed in plasma cells from 45 normal bone marrow donors or 10 Waldenstrom's macroglobulinemia, a related plasma cells malignancy that lacks bone disease. These data indicate that these factors are important mediators of multiple myeloma bone disease, and inhibitors of these proteins may be used to block bone disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 12 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:165307 USPATFULL
TITLE: Lectin compositions and methods for modulating an immune response to an antigen
INVENTOR(S): Segal, Andrew H., Boston, MA, UNITED STATES
Young, Elihu, Sharon, MA, UNITED STATES
PATENT ASSIGNEE(S): Genitrix, LLC (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004126793	A1	20040701
APPLICATION INFO.:	US 2003-666885	A1	20030919 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING

	NUMBER	DATE

PRIORITY INFORMATION: US 2002-404823P 20020820 (60)
US 2003-487407P 20030715 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE, BOSTON, MA, 02199
NUMBER OF CLAIMS: 147
EXEMPLARY CLAIM: 1
LINE COUNT: 28979
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 13 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:164872 USPATFULL
TITLE: Lectin compositions and methods for modulating an immune response to an antigen
INVENTOR(S): Segal, Andrew H., Boston, MA, UNITED STATES
Young, Elihu, Sharon, MA, UNITED STATES
PATENT ASSIGNEE(S): Genitrix, LLC (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004126357	A1	20040701
APPLICATION INFO.:	US 2003-666886	A1	20030919 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-404823P	20020820 (60)
	US 2003-487407P	20030715 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE, BOSTON, MA, 02199
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 39007
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 14 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:51429 USPATFULL
TITLE: Reagents and methods for modulating dkk-mediated interactions
INVENTOR(S): Allen, Kristina M., Hopkinton, MA, UNITED STATES
Anisowicz, Anthony, West Newton, MA, UNITED STATES
Damagnez, Veronique, Framingham, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004038860	A1	20040226
APPLICATION INFO.:	US 2002-182936	A1	20020802 (10)
	WO 2002-US15982		20020517

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 114
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Page(s)
LINE COUNT: 5224
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides reagents, compounds, compositions, and methods relating to novel interactions of the extracellular domain of ***LRP5*** , HBM (a variant of ***LRP5***), and/or LRP6 with Dkk, including Dkk-1. The various nucleic acids, polypeptides, antibodies, assay methods, diagnostic methods, and methods of treatment of the present invention are related to and impact on Dkk, ***LRP5*** , LRP6, HBM, and Wnt signaling. Dkk, ***LRP5*** , LRP6, HBM, and Wnt are implicated in bone and lipid cellular signaling. Thus, the present invention provides reagents and methods for modulating lipid levels

and/or bone mass and is useful in the treatment and diagnosis of
abnormal lipid levels and bone mass disorders, such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 15 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:44501 USPATFULL
TITLE: Proteins and nucleic acids encoding same
INVENTOR(S): Tchernev, Velizar T., Branford, CT, UNITED STATES
Spytek, Kimberly A., New Haven, CT, UNITED STATES
Zerhusen, Bryan D., Branford, CT, UNITED STATES
Patturajan, Meera, Branford, CT, UNITED STATES
Shimkets, Richard A., West Haven, CT, UNITED STATES
Li, Li, Branford, CT, UNITED STATES
Gangolli, Esha A., Madison, CT, UNITED STATES
Padigaru, Muralidhara, Branford, CT, UNITED STATES
Anderson, David W., Branford, CT, UNITED STATES
Rastelli, Luca, Guilford, CT, UNITED STATES
Miller, Charles E., Hill Drive, CT, UNITED STATES
Gerlach, Valerie, Branford, CT, UNITED STATES
Taupier, Raymond J., JR., East Haven, CT, UNITED STATES
Gusev, Vladimir Y., UNITED STATES
Colman, Steven D., Guilford, CT, UNITED STATES
Wolenc, Adam Ryan, New Haven, CT, UNITED STATES
Pena, Carol E. A., Guilford, CT, UNITED STATES
Furtak, Katarzyna, Anosia, CT, UNITED STATES
Grosse, William M., Bransford, CT, UNITED STATES
Alsobrook, John P., II, Madison, CT, UNITED STATES
Lepley, Denise M., Branford, CT, UNITED STATES
Rieger, Daniel K., Branford, CT, UNITED STATES
Burgess, Catherine E., Wethersfield, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004033493	A1	20040219
APPLICATION INFO.:	US 2002-72012	A1	20020131 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-267459P	20010208 (60)
	US 2001-266975P	20010207 (60)
	US 2001-267057P	20010207 (60)
	US 2001-266767P	20010205 (60)
	US 2001-266406P	20010202 (60)
	US 2001-265395P	20010131 (60)
	US 2001-265412P	20010131 (60)
	US 2001-265517P	20010131 (60)
	US 2001-265514P	20010131 (60)
	US 2001-267823P	20010209 (60)
	US 2001-268974P	20010215 (60)
	US 2001-271855P	20010227 (60)
	US 2001-271839P	20010227 (60)
	US 2001-273046P	20010302 (60)
	US 2001-272788P	20010302 (60)
	US 2001-275989P	20010314 (60)
	US 2001-275925P	20010314 (60)
	US 2001-275947P	20010314 (60)
	US 2001-275950P	20010314 (60)
	US 2001-276450P	20010315 (60)
	US 2001-276448P	20010315 (60)
	US 2001-276397P	20010316 (60)
	US 2001-276768P	20010316 (60)
	US 2001-278652P	20010320 (60)
	US 2001-278775P	20010326 (60)
	US 2001-278778P	20010326 (60)
	US 2001-279882P	20010329 (60)
	US 2001-279884P	20010329 (60)
	US 2001-280147P	20010330 (60)
	US 2001-283083P	20010411 (60)
	US 2001-282992P	20010411 (60)
	US 2001-285133P	20010420 (60)
	US 2001-285749P	20010423 (60)
	US 2001-288327P	20010503 (60)
	US 2001-288504P	20010503 (60)
	US 2001-294047P	20010529 (60)
	US 2001-294473P	20010530 (60)
	US 2001-296964P	20010608 (60)
	US 2001-298959P	20010618 (60)
	US 2001-299324P	20010619 (60)
	US 2001-312020P	20010813 (60)
	US 2001-312908P	20010816 (60)
	US 2001-312889P	20010816 (60)
	US 2001-313930P	20010821 (60)
	US 2001-315470P	20010828 (60)
	US 2001-316447P	20010831 (60)
	US 2001-318115P	20010907 (60)
	US 2001-318118P	20010907 (60)
	US 2001-318740P	20010912 (60)
	US 2001-323379P	20010919 (60)
	US 2001-330308P	20011018 (60)
	US 2001-330245P	20011018 (60)
	US 2001-332701P	20011114 (60)
	US 2001-271664P	20010226 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Ivor R. Elrifi, Ph.D., Mintz, Levin, Cohn, Ferris,,
Glovsky and Popeo, P.C., One Financial Center, Boston,
MA, 02111
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
LINE COUNT: 59681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein are nucleic acid sequences that encode novel
polypeptides. Also disclosed are polypeptides encoded by these nucleic
acid sequences, and antibodies, which immunospecifically-bind to the
polypeptide, as well as derivatives, variants, mutants, or fragments of

the aforementioned polypeptide, polynucleotide, or antibody. The
invention further discloses therapeutic, diagnostic and research methods
for diagnosis, treatment, and prevention of disorders involving any one
of these novel human nucleic acids and proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 16 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:31217 USPATFULL
TITLE: Wise/Sost nucleic acid sequences and amino acid
sequences
INVENTOR(S): Krumlauf, Robb, Mission Hills, KS, UNITED STATES
Ellies, Debra, Kansas City, MO, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004023356	A1	20040205
APPLICATION INFO.:	US 2003-464368	A1	20030616 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-388970P	20020614 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: POLSINELLI SHALTON & WELTE, P.C., Suite 1000, 700 W.
47th Street, Kansas City, MO, 64108
NUMBER OF CLAIMS: 235
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 4672
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to nucleic acid sequences and amino acid
sequences which influence bone deposition, the Wnt pathway, ocular
development, tooth development, and may bind to LRP. The nucleic acid
sequence and polypeptides include Wise and Sost as well as a family of
molecules which express a cysteine knot polypeptide. Additionally, the
present invention relates to various molecular tools derived from the
nucleic acids and polypeptides including vectors, transfected host
cells, monochronal antibodies, Fab fragments, and methods for impacting
the pathways.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 17 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:18907 USPATFULL
TITLE: Compositions and methods for modulating cell
differentiation
INVENTOR(S): Lassar, Andrew B., Newton Center, MA, UNITED STATES
Mercola, Mark, Del Mar, CA, UNITED STATES
Gupta, Ruchika, San Diego, CA, UNITED STATES
Marvin, Martha, Brookline, MA, UNITED STATES
Schneider, Valerie, Philadelphia, PA, UNITED STATES
Tzahor, Eldad, Brookline, MA, UNITED STATES
Brott, Barbara, Boston, MA, UNITED STATES
Sokol, Sergei, Boston, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004014209	A1	20040122
APPLICATION INFO.:	US 2003-351275	A1	20030123 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-351126P	20020123 (60)
	US 2002-352456P	20020128 (60)
	US 2002-352665P	20020129 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FOLEY HOAG, LLP, PATENT GROUP, WORLD TRADE CENTER WEST,
155 SEAPORT BLVD, BOSTON, MA, 02110
NUMBER OF CLAIMS: 61
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 24 Drawing Page(s)
LINE COUNT: 4008
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compositions and methods for
stimulating differentiation of stem cells into cardiac cells. The
methods of the invention involve contacting a population cells
comprising stem cells with at least one Wnt antagonist, such as a
polypeptide or polypeptide fragment. In certain embodiments, the methods
of the invention involve Dkk proteins or fragments, homologs,
derivatives, variants, or peptidomimetics thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 18 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:13385 USPATFULL
TITLE: Proteins and nucleic acids encoding same
INVENTOR(S): Alsobrook, John P., II, Madison, CT, UNITED STATES
Anderson, David W., Branford, CT, UNITED STATES
Ballinger, Robert A., Newington, CT, UNITED STATES
Boldog, Ference L., North Haven, CT, UNITED STATES
Burgess, Catherine E., Wethersfield, CT, UNITED STATES
Casman, Stacie J., North Haven, CT, UNITED STATES

Ellerman, Karen, Branford, CT, UNITED STATES
Gangolli, Esha A., Madison, CT, UNITED STATES
Gerlach, Valerie, Branford, CT, UNITED STATES
Gilbert, Jennifer A., Madison, CT, UNITED STATES
Gorman, Linda, Branford, CT, UNITED STATES
Guo, Xiaojia (Sasha), Branford, CT, UNITED STATES
Gusev, Vladimir Y., Madison, CT, UNITED STATES
Kekuda, Ramesh, Norwalk, CT, UNITED STATES
Li, Li, Branford, CT, UNITED STATES
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Padigaru, Muralidhara, Branford, CT, UNITED STATES
Patturajan, Meera, Branford, CT, UNITED STATES
A. Pena, Carol E., New Haven, CT, UNITED STATES
Peyman, John A., New Haven, CT, UNITED STATES
Rastelli, Luca, Guilford, CT, UNITED STATES
Shenoy, Suresh G., Branford, CT, UNITED STATES
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Smithson, Glennda, Guilford, CT, UNITED STATES
Spytek, Kimberly A., New Haven, CT, UNITED STATES
Stone, David J., Guilford, CT, UNITED STATES
Taupier, Raymond J., JR., East Haven, CT, UNITED STATES
Tchernev, Velizar T., Branford, CT, UNITED STATES
Vernet, Corine A.M., Branford, CT, UNITED STATES
Zerhusen, Bryan D., Branford, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004009907	A1	20040115
APPLICATION INFO.:	US 2002-85198	A1	20020225 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-271646P	20010226 (60)
	US 2001-276401P	20010316 (60)
	US 2001-311981P	20010813 (60)
	US 2001-312858P	20010816 (60)
	US 2001-271840P	20010227 (60)
	US 2001-277324P	20010320 (60)
	US 2001-286096P	20010424 (60)
	US 2001-299695P	20010620 (60)
	US 2001-315614P	20010829 (60)
	US 2001-272405P	20010228 (60)
	US 2001-272410P	20010228 (60)
	US 2001-272414P	20010228 (60)
	US 2001-278660P	20010320 (60)
	US 2001-280234P	20010330 (60)
	US 2001-272404P	20010228 (60)
	US 2001-280039P	20010330 (60)
	US 2001-313280P	20010817 (60)
	US 2001-322818P	20010917 (60)
	US 2001-273300P	20010302 (60)
	US 2001-280818P	20010402 (60)
	US 2001-288353P	20010503 (60)
	US 2001-294834P	20010531 (60)
	US 2001-299845P	20010621 (60)
	US 2001-272922P	20010302 (60)
	US 2001-272787P	20010302 (60)
	US 2001-285754P	20010423 (60)
	US 2001-303242P	20010705 (60)
	US 2001-273048P	20010302 (60)
	US 2001-283443P	20010412 (60)
	US 2001-291703P	20010517 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Ivor R. Elrifi, MINTZ, LEVIN, COHN, FERRIS,, GLOVSKY and POPEO, P.C., One Financial Center, Boston, MA, 02111
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
LINE COUNT: 46330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein are nucleic acid sequences that encode novel polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 19 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:13003 USPATFULL
TITLE: Diagnosis, prognosis and identification of potential therapeutic targets of multiple myeloma based on gene expression profiling
INVENTOR(S): Shaughnessy, John D., Little Rock, AR, UNITED STATES
Zhan, Fenghuang, Little Rock, AR, UNITED STATES
Barlogie, Bart, Little Rock, AR, UNITED STATES

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2004009523 A1 20040115
APPLICATION INFO.: US 2003-454263 A1 20030604 (10)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-409004, filed
on 8 Apr 2003, PENDING Continuation-in-part of Ser. No.
US 2002-289746, filed on 7 Nov 2002, PENDING

NUMBER	DATE
PRIORITY INFORMATION: US 2002-403075P	20020813 (60)
US 2001-348238P	20011107 (60)
US 2002-355386P	20020208 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle
Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 24 Drawing Page(s)
LINE COUNT: 4510
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gene expression profiling between normal B cells/plasma cells and
multiple myeloma cells revealed four distinct subgroups of multiple
myeloma plasma cells that have significant correlation with clinical
characteristics known to be associated with poor prognosis. Diagnosis
for multiple myeloma (and possibly monoclonal gammopathy of undetermined
significance) based on differential expression of 14 genes, as well as
prognostics for the four subgroups of multiple myeloma based on the
expression of 24 genes were also established. Gene expression profiling
also allows placing multiple myeloma into a developmental schema
parallel to that of normal plasma cell differentiation. The development
of a gene expression- or developmental stage-based classification system
for multiple myeloma would lead to rational design of more accurate and
sensitive diagnostics, prognostics and tumor-specific therapies for
multiple myeloma.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 20 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:211474 USPATFULL
TITLE: High bone mass gene of 1.1q13.3
INVENTOR(S): Carulli, John P., Southboro, MA, United States
Little, Randall D., Newtonville, MA, United States
Recker, Robert R., Omaha, NE, United States
Johnson, Mark L., Omaha, NE, United States

PATENT ASSIGNEE(S): Genome Therapeutics Corporation, Waltham, MA, United
States (U.S. corporation)

NUMBER	KIND	DATE
PATENT INFORMATION: US 6780609	B1	20040824
APPLICATION INFO.: US 2000-543771		20000405 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-229319, filed
on 13 Jan 1999, now abandoned

NUMBER	DATE
PRIORITY INFORMATION: US 1998-105511P	19981023 (60)
US 1998-71449P	19980113 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Fredman, Jeffrey
ASSISTANT EXAMINER: Kaushal, Sumesh
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 36 Drawing Figure(s); 32 Drawing Page(s)
LINE COUNT: 11922
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to isolate
and detect a high bone mass gene and a corresponding wild-type gene, and
mutants thereof. The present invention also relates to the high bone
mass gene, the corresponding wild-type gene, and mutants thereof. The
genes identified in the present invention are implicated in bone
development. The invention also provides nucleic acids, including coding
sequences, oligonucleotide primers and probes, proteins, cloning
vectors, expression vectors, transformed hosts, methods of developing
pharmaceutical compositions, methods of identifying molecules involved
in bone development, and methods of diagnosing and treating diseases
involved in bone development. In preferred embodiments, the present
invention is directed to methods for treating, diagnosing and preventing
osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 21 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2004:192608 USPATFULL
TITLE: High bone mass gene of 11q13.3
INVENTOR(S): Carulli, John P., Southboro, MA, United States
Little, Randall D., Newtonville, MA, United States
Recker, Robert R., Omaha, NE, United States

Johnson, Mark L., Omaha, NE, United States
PATENT ASSIGNEE(S): Genome Therapeutics Corporation, Waltham, MA, United
States (U.S. corporation)
Creighton University School of Medicine, Omaha, NE,
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6770461	B1	20040803
APPLICATION INFO.:	US 2000-544398		20000405 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-229319, filed
on 13 Jan 1999

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105511P	19981023 (60)
	US 1998-71449P	19980113 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Falk, Anne-Marie
ASSISTANT EXAMINER: Qian, Celine
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 36 Drawing Figure(s); 32 Drawing Page(s)
LINE COUNT: 11938
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to isolate
and detect a high bone mass gene and a corresponding wild-type gene, and
mutants thereof. The present invention also relates to the high bone
mass gene, the corresponding wild-type gene, and mutants thereof The
genes identified in the present invention are implicated in bone
development. The invention also provides nucleic acids, including coding
sequences, oligonucleotide primers and probes, proteins, cloning
vectors, expression vectors, transformed hosts, methods of developing
pharmaceutical compositions, methods of identifying molecules involved
in bone development, and methods of diagnosing and treating diseases
involved in bone development. In preferred embodiments, the present
invention is directed to methods for treating, diagnosing and preventing
osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 22 OF 45 MEDLINE on STN
DUPLICATE 1
ACCESSION NUMBER: 2004244690 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15143163
TITLE: The ***LRP5*** high-bone-mass G171V mutation disrupts
LRP5 interaction with Mesd.
AUTHOR: Zhang Yazhou; Wang Yang; Li Xiaofeng; Zhang Jianhong; Mao
Junhao; Li Zhong; Zheng Jie; Li Lin; Harris Steve; Wu
Dianqing
CORPORATE SOURCE: Department of Genetics and Developmental Biology,
University of Connecticut Health Center, 263 Farmington
Ave., Farmington, CT 06410, USA.
CONTRACT NUMBER: CA85420 (NCI)
GM54167 (NIGMS)
SOURCE: Molecular and cellular biology, (2004 Jun) 24 (11) 4677-84.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040515
Last Updated on STN: 20040624
Entered Medline: 20040621
AB The mechanism by which the high-bone-mass (HBM) mutation (G171V) of the
Wnt coreceptor ***LRP5*** regulates canonical Wnt signaling was
investigated. The mutation was previously shown to reduce DKK1-mediated
antagonism, suggesting that the first YWTD repeat domain where G171 is
located may be responsible for DKK-mediated antagonism. However, we found
that the third YWTD repeat, but not the first repeat domain, is required
for DKK1-mediated antagonism. Instead, we found that the G171V mutation
disrupted the interaction of ***LRP5*** with Mesd, a chaperone protein
for ***LRP5*** /6 that is required for transport of the coreceptors to
cell surfaces, resulting in fewer ***LRP5*** molecules on the cell
surface. Although the reduction in the number of cell surface
LRP5 molecules led to a reduction in Wnt signaling in a paracrine
paradigm, the mutation did not appear to affect the activity of
coexpressed Wnt in an autocrine paradigm. Together with the observation
that osteoblast cells produce autocrine canonical Wnt, Wnt7b, and that
osteocytes produce paracrine DKK1, we think that the G171V mutation may
cause an increase in Wnt activity in ***osteoblasts*** by reducing the
number of targets for paracrine DKK1 to antagonize without affecting the
activity of autocrine Wnt.

L5 ANSWER 23 OF 45 MEDLINE on STN
DUPLICATE 2
ACCESSION NUMBER: 2004212083 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15110782
TITLE: Glucocorticoid enhances the expression of dickkopf-1 in

human ***osteoblasts*** : novel mechanism of
glucocorticoid-induced osteoporosis.
AUTHOR: Ohnaka Keizo; Taniguchi Hiroshi; Kawate Hisaya; Nawata
Hajime; Takayanagi Ryoichi
CORPORATE SOURCE: Department of Geriatric Medicine, Graduate School of
Medical Sciences, Kyushu University, 3-1-1 Maidashi,
Higashi-ku, Fukuoka 812-8582, Japan..
oonaka@geriat.med.kyushu-u.ac.jp
SOURCE: Biochemical and biophysical research communications, (2004
May 21) 318 (1) 259-64.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040428
Last Updated on STN: 20040609
Entered Medline: 20040608
AB To clarify the underlying mechanism of glucocorticoid-induced
osteoporosis, we investigated the effect of glucocorticoid on the
expression of dickkopf-1 (Dkk-1), an antagonist of Wnt signaling, in
primary cultured human ***osteoblasts*** . Dexamethasone markedly
induced the expression of mRNA for Dkk-1 in a dose- and time-dependent
manner. The expression of Kremen1, a receptor for Dkk, did not change by
the treatment with dexamethasone, while that of low-density lipoprotein
receptor-related protein 5 (***LRP5***), a Wnt coreceptor, slightly
decreased by the treatment with dexamethasone. Dexamethasone increased
the transcriptional activity of the Dkk-1 gene promoter in human
osteoblasts . Serial deletion and mutation analyses of the Dkk-1
promoter showed that one putative glucocorticoid responsive element-like
sequence located from -788 to -774bp is essential for the enhancement of
the Dkk-1 promoter activity by dexamethasone in human ***osteoblasts***
. Since the Wnt signal is now recognized as a crucial regulator for bone
formation, the Dkk-1 enhanced by glucocorticoid may inhibit the Wnt signal
in ***osteoblasts*** , which may be involved in the pathogenesis of
glucocorticoid-induced osteoporosis.

L5 ANSWER 24 OF 45 MEDLINE on STN
ACCESSION NUMBER: 2004199481 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15095618
TITLE: [Wnt/ ***LRP5*** , a new regulation osteoblastic pathway
involved in reaching peak bone masses].
Wnt/ ***LRP5*** , une nouvelle voie de regulation
osteoblastique impliquee dans l'acquisition du pic de
masses osseuses.
AUTHOR: Caverzasio Joseph
CORPORATE SOURCE: Service des maladies osseuses Departement de rehabilitation
et geriatrie HUG..
Joseph.Caverzasio@medecine.unige.ch
SOURCE: Revue medicale de la Suisse romande, (2004 Feb) 124 (2)
81-2.
Journal code: 0421524. ISSN: 0035-3655.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040421
Last Updated on STN: 20040521
Entered Medline: 20040520
AB With the ageing of the population in industrial countries, osteoporosis
became an important concern of public health. For an efficacious
treatment of this disease, we would need drugs capable of selectively and
safely increasing bone volume. Recent genetic analyses revealed a new
signaling pathway involved in the regulation of osteoblastic cells and the
acquisition of pic bone mass. Loss or gain of function mutations in the
LRP5 gene have been found to be associated with correspondingly
low or high bone mass syndromes. Loss of function is associated with
juvenile osteoporosis, whereas gain of function leads to the high bone
mass syndrome. Recent studies have shown that ***LRP5*** is
implicated in the regulation of the proliferation and of the activity of
osteoblastic cells. By analogy with other cellular systems, it has been
suggested that ***LRP5*** plays a role in the Wnt signaling system.
Wnt proteins are known to be involved in developmental processes and the
implication of this system in controlling osteoblastic activity and bone
formation was completely unexpected. Analysis of the cellular mechanism
by which Wnt/ ***LRP5*** activates osteoblastic cells is of potential
interest for the development of new molecules capable of selectively
increasing bone mass for the treatment of osteoporosis.

L5 ANSWER 25 OF 45 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004505926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15474285
TITLE: Wnt signaling in ***osteoblasts*** and bone diseases.
AUTHOR: Westendorf Jennifer J; Kahler Rachel A; Schroeder Tania M
CORPORATE SOURCE: The Cancer Center and Department of Orthopaedic Surgery,

University of Minnesota, MMC 806, 420 Delaware St. SE,
Minneapolis, MN 55455, USA..
weste047@umn.edu
SOURCE: Gene, (2004 Oct 27) 341 19-39. Ref: 219
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20041013
Last Updated on STN: 20050114
Entered Medline: 20050113
AB Recent revelations that the canonical Wnt signaling pathway promotes
postnatal bone accrual are major advances in our understanding of skeletal
biology and bring tremendous promise for new therapeutic treatments for
osteoporosis and other diseases of altered bone mass. Wnts are soluble
glycoproteins that engage receptor complexes composed of ***Lrp5*** /6
and Frizzled proteins. A subgroup of Wnts induces a cascade of
intracellular events that stabilize beta-catenin, facilitating its
transport to nuclei where it binds Lef1/Tcf transcription factors and
alters gene expression to promote osteoblast expansion and function.
Natural extracellular Wnt antagonists, Dickkopfs and secreted
frizzled-related proteins, impair osteoblast function and block bone
formation. In several genetic disorders of altered skeletal mass,
mutations in ***LRP5*** create gain-of-function or loss-of-function
receptors that are resistant to normal regulatory mechanisms and cause
higher or lower bone density, respectively. In this review, we summarize
the available molecular, cellular, and genetic data that demonstrate how
Lrp5 and other components of the Wnt signaling pathway influence
osteoblast proliferation, function, and survival. We also discuss
regulatory mechanisms discovered in developmental and tumor models that
may provide insights into novel therapies for bone diseases.

L5 ANSWER 26 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2003:330153 USPATFULL
TITLE: Diagnosis, prognosis and identification of potential
therapeutic targets of multiple myeloma based on gene
expression profiling
INVENTOR(S): Shaughnessy, John D., Little Rock, AR, UNITED STATES
Barlogie, Bart, Little Rock, AR, UNITED STATES
Zhan, Fenghuang, Little Rock, AR, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003232364	A1	20031218
APPLICATION INFO.:	US 2003-409004	A1	20030408 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-289746, filed
on 7 Nov 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-403075P	20020813 (60)
	US 2001-348238P	20011107 (60)
	US 2002-355386P	20020208 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Dr. Benjamin Adler, ADLER & ASSOCIATES, 8011 Candle
Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 4100
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gene expression profiling between normal B cells/plasma cells and
multiple myeloma cells revealed four distinct subgroups of multiple
myeloma plasma cells that have significant correlation with clinical
characteristics known to be associated with poor prognosis. Diagnosis
for multiple myeloma (and possibly monoclonal gammopathy of undetermined
significance) based on differential expression of 14 genes, as well as
prognostics for the four subgroups of multiple myeloma based on the
expression of 24 genes were also established. Gene expression profiling
also allows placing multiple myeloma into a developmental schema
parallel to that of normal plasma cell differentiation. The development
of a gene expression- or developmental stage-based classification system
for multiple myeloma would lead to rational design of more accurate and
sensitive diagnostics, prognostics and tumor-specific therapies for
multiple myeloma.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 27 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2003:312196 USPATFULL
TITLE: High bone mass gene of 11q13.3
INVENTOR(S): Carulli, John P., Southboro, MA, UNITED STATES
Recker, Robert R., Omaha, NE, UNITED STATES

Johnson, Mark L., Omaha, NE, UNITED STATES
Little, Randall D., Newtonville, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003219793	A1	20031127
APPLICATION INFO.:	US 2003-374979	A1	20030228 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2002-240851, filed on 4 Oct 2002, PENDING A 371 of International Ser. No. WO 2000-US16951, filed on 21 Jun 2000, PENDING A 371 of International Ser. No. US 2000-578900, filed on 26 May 2000, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Estelle J. Tsevdos, Esq., KENYON & KENYON, One Broadway, New York, NY, 10004
NUMBER OF CLAIMS: 117
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 31 Drawing Page(s)
LINE COUNT: 5096
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to isolate and detect a high bone mass gene and a corresponding wild-type gene, and mutants thereof. The present invention also relates to the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The genes identified in the present invention are implicated in bone development and in focal adhesion signaling. The invention also provides nucleic acids, including coding sequences, oligonucleotide primers and probes, proteins, cloning vectors, expression vectors, transformed hosts, methods of developing pharmaceutical compositions, methods of identifying molecules involved in bone development, and methods of diagnosing and treating diseases involved in bone development. In preferred embodiments, the present invention is directed to methods for treating, diagnosing and preventing osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 28 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2003:237343 USPATFULL
TITLE: Wnt and frizzled receptors as targets for immunotherapy in head and neck squamous cell carcinomas
INVENTOR(S): Rhee, Chae-Seo, Seoul, KOREA, REPUBLIC OF
Sen, Malini, San Diego, CA, UNITED STATES
Wu, Christina, San Diego, CA, UNITED STATES
Leoni, Lorenzo M., San Diego, CA, UNITED STATES
Corr, Maripat, San Diego, CA, UNITED STATES
Carson, Dennis A., Del Mar, CA, UNITED STATES
PATENT ASSIGNEE(S): REGENTS OF THE UNIVERSITY OF CALIFORNIA, Oakland, CA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003165500	A1	20030904
APPLICATION INFO.:	US 2002-285976	A1	20021101 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2002-US13802, filed on 1 May 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-287995P	20010501 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 140
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Page(s)
LINE COUNT: 7969
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The diverse receptor-ligand pairs of the Wnt and frizzled (Fzd) families play important roles during embryonic development, and thus may be overexpressed in cancers that arise from immature cells. The mRNA levels and expression levels of 5 Wnt (Wnt-1, 5a, 7a, 10b, 13) and 2 Fzd (Fzd-2, 5) genes in 10 head and neck squamous carcinoma cell lines (HNSCC) were investigated. In addition, anti-Wnt-1 antibodies were used to study the Wnt/Fzd signalling pathway. These results indicate that HNSCC cell lines overexpress one or more Wnt and Fzd genes, and the proliferation and survival of a subset of HNSCC may depend on the Wnt/Fzd pathway. Therefore, the Wnt and Fzd receptors may be useful targets for immunotherapy of this common cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 29 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2003:187400 USPATFULL
TITLE: Compositions and methods for modulating blood-brain barrier transport
INVENTOR(S): Beliveau, Richard, Quebec, CANADA

Demeule, Michel, Montreal, CANADA
Yang, Joseph, North Delta, CANADA
Kennard, Malcolm L., North Vancouver, CANADA
Gabathuler, Reinhard, Vancouver, CANADA
PATENT ASSIGNEE(S): BioMarin Pharmaceutical Inc., Novato, CA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003129186	A1	20030710
APPLICATION INFO.:	US 2002-206448	A1	20020725 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-308002P	20010725 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 44 Drawing Page(s)
LINE COUNT: 3332
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides conjugates of therapeutic or active agents with melanotransferrin or with other ligands of a melanotransferrin receptor, melanotransferrin receptor modulators, and related compositions and methods for modulating blood-brain barrier transport by providing methods of screening and selecting such conjugates, ligands, and modulators in vitro and in vivo, and methods of use of such conjugates, modulators and ligands in diagnosis and the treatment of diseases, including particularly diseases of the central nervous system or lysosomal storage diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 30 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2003:173952 USPATFULL
TITLE: Bone anabolic compounds and methods of use
INVENTOR(S): Manolagas, Stavros C., Little Rock, AR, UNITED STATES
Katzenellenbogen, John A., Urbana, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003119800	A1	20030626
APPLICATION INFO.:	US 2002-165380	A1	20020607 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-299009P	20010618 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614
NUMBER OF CLAIMS: 84
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 31 Drawing Page(s)
LINE COUNT: 3219
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A variety of bone anabolic compounds are useful for maintaining and/or increasing bone mass, density, and/or strength in mammals. Preferred compounds enhance bone anabolic activity while minimizing or eliminating undesirable feminizing or masculinizing effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 31 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2003:37506 USPATFULL
TITLE: Regulator gene and system useful for the diagnosis and therapy of osteoporosis
INVENTOR(S): Warman, Matthew L., Shaker Heights, OH, UNITED STATES
Gong, Yaoqin, Jinan, CHINA
Olsen, Bjorn R., Milton, MA, UNITED STATES
Rawadi, Georges, Paris, FRANCE
Roman-Roman, Sergio, Paris, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003027151	A1	20030206
APPLICATION INFO.:	US 2001-931375	A1	20010817 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-304851P	20010713 (60)
	US 2000-226119P	20000818 (60)
	US 2000-234337P	20000922 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 3896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A bone strength and mineralization regulatory ("BSMR") protein is provided that can exist in multiple forms and that affects bone density.
Polymorphic gene sequences of the protein are provided that are diagnostic of predipostion to osteoporosis. Other detection tools,

compositions and methods of their use also are provided for predicting, evaluating and altering bone strength and mineralization status. The invention provides new natural and synthetic pharmaceuticals that effect the BSMR regulatory pathway and improve bone status. Tools also are provided for finding new pharmaceuticals that operate by binding to BSMR and that activate and/or deactivate this protein's biological function related to osteoporosis and blood vessel formation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 32 OF 45 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003149709 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12551949
TITLE: Lymphoid enhancer factor-1 and beta-catenin inhibit Runx2-dependent transcriptional activation of the osteocalcin promoter.
AUTHOR: Kahler Rachel A; Westendorf Jennifer J
CORPORATE SOURCE: University of Minnesota Cancer Center, Department of Orthopaedic Surgery and Graduate Program in Microbiology, Immunology and Cancer Biology, Minneapolis, Minnesota 55455, USA.
SOURCE: Journal of biological chemistry, (2003 Apr 4) 278 (14) 11937-44.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030401
Last Updated on STN: 20030520
Entered Medline: 20030519
AB Functional control of the transcription factor Runx2 is crucial for normal bone formation. Runx2 is detectable throughout osteoblast development and maturation and temporally regulates several bone-specific genes. In this study, we identified a novel post-translational mechanism regulating Runx2-dependent activation of the osteocalcin promoter. A functional binding site for the high mobility group protein lymphoid enhancer-binding factor 1 (LEF1) was found adjacent to the proximal Runx2-binding site in the osteocalcin promoter. In transcription assays, LEF1 repressed Runx2-induced activation of the mouse osteocalcin 2 promoter in several osteoblast lineage cell lines. Mutations in the LEF1-binding site increased the basal activity of the osteocalcin promoter; however, the LEF1 recognition site in the osteocalcin promoter was surprisingly not required for LEF1 repression. A novel interaction between the DNA-binding domains of Runx2 and LEF1 was identified and found crucial for LEF1-mediated repression of Runx2. LEF1 is a nuclear effector of the Wnt/ ***LRP5*** /beta-catenin signaling pathway, which is also essential for osteoblast proliferation and normal skeletal development. A constitutively active beta-catenin enhanced LEF1-dependent repression of Runx2. These data identify a novel mechanism of regulating Runx2 activity in ***osteoblasts*** and link Runx2 transcriptional activity to beta-catenin signaling.

L5 ANSWER 33 OF 45 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003508144 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14584895
TITLE: BMP-2 controls alkaline phosphatase expression and osteoblast mineralization by a Wnt autocrine loop.
AUTHOR: Rawadi Georges; Vayssiere Beatrice; Dunn Fred; Baron Roland; Roman-Roman Sergio
CORPORATE SOURCE: Proskelia Pharmaceuticals, Romainville, France.. georges.rawadi@proskelia.com
SOURCE: Journal of bone and mineral research : official journal of the American Society for Bone and Mineral Research, (2003 Oct) 18 (10) 1842-53.
Journal code: 8610640. ISSN: 0884-0431.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20031031
Last Updated on STN: 20040603
Entered Medline: 20040602
AB Wnt/beta-catenin signaling has recently been suggested to be involved in bone biology. The precise role of this cascade in osteoblast differentiation was examined. We show that a Wnt autocrine loop mediates the induction of alkaline phosphatase and mineralization by BMP-2 in pre-osteoblastic cells. INTRODUCTION: Loss of function of ***LRP5*** leads to osteoporosis (OPPG syndrome), and a specific point mutation in this same receptor results in high bone mass (HBM). Because ***LRP5*** acts as a coreceptor for Wnt proteins, these findings suggest a crucial role for Wnt signaling in bone biology. MATERIALS AND METHODS: We have investigated the involvement of the Wnt/ ***LRP5*** cascade in

osteoblast function by using the pluripotent mesenchymal cell lines
C3H10T1/2, C2C12, and ST2 and the osteoblast cell line MC3T3-E1.
Transfection experiments were carried out with a number of elements of the
Wnt/ ***LRP5*** pathway. Measuring osteoblast and adipocyte
differentiation markers addressed the effect of this cascade on osteoblast
differentiation. RESULTS: In mesenchymal cells, only Wnt's capable of
stabilizing beta-catenin induced the expression of alkaline phosphatase
(ALP). Wnt3a-mediated ALP induction was inhibited by overexpression of
either Xddl, dickkopf 1 (dkk1), or LRP5deltaC, indicating that canonical
beta-catenin signaling is responsible for this activity. The use of
Noggin, a bone morphogenic protein (BMP) inhibitor, or cyclopamine, a
Hedgehog inhibitor, revealed that the induction of ALP by Wnt is
independent of these morphogenetic proteins and does not require de novo
protein synthesis. In contrast, blocking Wnt/ ***LRP5*** signaling or
protein synthesis inhibited the ability of both BMP-2 and Shh to induce
ALP in mesenchymal cells. Moreover, BMP-2 enhanced Wntl and Wnt3a
expression in our cells. In MC3T3-E1 cells, where endogenous ALP levels
are maximal, antagonizing the Wnt/ ***LRP5*** pathway led to a decrease
of ALP activity. In addition, overexpression of dkkl reduced
extracellular matrix mineralization in a BMP-2-dependent assay.
CONCLUSIONS: Our data strongly suggest that the capacity of BMP-2 and Shh
to induce ALP relies on Wnt expression and the Wnt/ ***LRP5***
signaling cascade. Moreover the effects of BMP-2 on extracellular matrix
mineralization by ***osteoblasts*** are mediated, at least in part, by
the induction of a Wnt autocrine/paracrine loop. These results may help
to explain the phenotype of OPPG patients and HBM.

L5 ANSWER 34 OF 45 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003290363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12817748
TITLE: High bone mass in mice expressing a mutant ***LRP5***
gene.
AUTHOR: Babij Philip; Zhao Weiguang; Small Clayton; Kharode
Yogendra; Yaworsky Paul J; Bouxsein Mary L; Reddy
Padmalatha S; Bodine Peter V N; Robinson John A; Bhat
Bheem; Marzolf James; Moran Robert A; Bex Frederick
CORPORATE SOURCE: Genomics, Wyeth Research, Andover, Massachusetts, USA.
SOURCE: Journal of bone and mineral research : official journal of
the American Society for Bone and Mineral Research, (2003
Jun) 18 (6) 960-74.
Journal code: 8610640. ISSN: 0884-0431.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20030624
Last Updated on STN: 20040212
Entered Medline: 20040211
AB A unique mutation in ***LRP5*** is associated with high bone mass in
man. Transgenic mice expressing this ***LRP5*** mutation have a
similar phenotype with high bone mass and enhanced strength. These
results underscore the importance of ***LRP5*** in skeletal regulation
and suggest targets for therapies for bone disease. A mutation (G171V) in
the low-density lipoprotein receptor related protein 5 (***LRP5***)
has been associated with high bone mass (HBM) in two independent human
kindreds. To validate the role of the mutation, several lines of
transgenic mice were created expressing either the human ***LRP5***
G171V substitution or the wildtype ***LRP5*** gene in bone.
Volumetric bone mineral density (vBMD) analysis by pQCT showed dramatic
increases in both total vBMD (30-55%) and trabecular vBMD (103-250%) of
the distal femoral metaphysis and increased cortical size of the femoral
diaphysis in mutant G171V transgenics at 5, 9, 17, 26, and 52 weeks of age
($p < 0.01$ for all). In addition, high-resolution microcomputed tomography
(microCT) analysis of the distal femorae and lumbar vertebrae revealed an
increase (110-232%) in trabecular bone volume fraction caused by both
increased trabecular number (41-74%) and increased trabecular thickness
(34-46%; $p < 0.01$ for all) in the mutant G171V mice. The increased bone
mass was associated with significant increases in vertebral compressive
strength (80-140%) and the increased cortical size with significant
increases in femoral bending strength (50-130%). There were no
differences in osteoclast number at 17 weeks of age. However, compared
with littermate controls, the mutant G171V transgenic mice showed an
increase in actively mineralizing bone surface, enhanced alkaline
phosphatase staining in ***osteoblasts*** , and a significant reduction
in the number of TUNEL-positive ***osteoblasts*** and osteocytes.

These results suggest that the increased bone mineral density in mutant
G171V mice was caused by increased numbers of active ***osteoblasts***
, which could in part be because of their increased functional lifespan.
While slight bone anabolic activity was observed from overexpression of
the wildtype ***LRP5*** gene, it is clear that the G171V mutation,
rather than overexpression of the receptor itself, is primarily
responsible for the dramatic HBM bone effects. Together, these findings
establish the importance of this novel and unexpected role of a
lipoprotein receptor in regulating bone mass and afford a new model to
explore ***LRP5*** and its recent association with Wnt signaling in
bone biology.

L5 ANSWER 35 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 2003:114750 BIOSIS
DOCUMENT NUMBER: PREV200300114750
TITLE: IGF-I and IGFBP-3 transport in the rat heart.
AUTHOR(S): Boes, Mary; Dake, Brian L.; Booth, Barbara A.; Sandra,
Alexander; Bateman, Mathew; Knudtson, Kevin L.; Bar, Robert
S. [Reprint Author]
CORPORATE SOURCE: Division of Endocrinology, Dept. of Internal Medicine,
Univ. of Iowa, Highway 6 West, 3E19 VA Medical Center, Iowa
City, IA, 52246, USA
rbar@icva.gov
SOURCE: American Journal of Physiology, (January 2003) Vol. 284,
No. 1 Part 1, pp. E237-E239. print.
ISSN: 0002-9513 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 2003
Last Updated on STN: 26 Feb 2003
AB Specific binding of IGF-binding protein (IGFBP)-3 was shown to be present
in the isolated, beating rat heart. The uptake of perfused 125I-labeled
IGF-I in the beating heart was decreased to 9% by blocking IGF-I binding
sites with the IGF-I analog Long R3 (***LR3***) IGF-I. When
LR3 was perfused with complexes of 125I-IGF-IcntdotIGFBP-3, uptake
of 125I-IGF-I was decreased to 41%, which was significantly greater than
LR3 and 125I-IGF-I (41 vs. 9%). These data suggest that both
microvessel IGF-I and IGFBP-3 binding sites contribute to the transport of
IGF-I in the perfused rat heart. This also suggests a novel and plausible
mechanism whereby circulating IGFs reach sites of IGF bioactivity.

L5 ANSWER 36 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 2003:507666 BIOSIS
DOCUMENT NUMBER: PREV200300509318
TITLE: Regulation of bone formation by Wnt signaling.
AUTHOR(S): Patel, M. S. [Reprint Author]; Glass, D. A. II [Reprint
Author]; Long, F.; Taketo, M. M.; McMahon, A. P.; Karsenty,
G. [Reprint Author]
CORPORATE SOURCE: Department of Molecular and Human Genetics, Baylor College
of Medicine, Houston, TX, USA
SOURCE: American Journal of Human Genetics, (November 2003) Vol.
73, No. 5, pp. 171. print.
Meeting Info.: 53rd Annual Meeting of the American Society
of Human Genetics. Los Angeles, CA, USA. November 04-08,
2003. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003

L5 ANSWER 37 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 2002:517776 BIOSIS
DOCUMENT NUMBER: PREV200200517776
TITLE: High bone density due to a mutation in ***LDL*** -
receptor - ***related*** ***protein***
5 : The authors reply.
AUTHOR(S): Boyden, Lynn [Reprint author]; Insogna, Karl [Reprint
author]; Lifton, Richard P. [Reprint author]
CORPORATE SOURCE: Yale University School of Medicine, New Haven, CT, 06510,
USA
richard.lifton@yale.edu
SOURCE: New England Journal of Medicine, (September 19, 2002) Vol.
347, No. 12, pp. 944. print.
CODEN: NEJMAG. ISSN: 0028-4793.
DOCUMENT TYPE: Letter
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

L5 ANSWER 38 OF 45 USPATFULL on STN
ACCESSION NUMBER: 2002:301758 USPATFULL
TITLE: Transgenic mice containing LPR5 gene disruptions
INVENTOR(S): Klein, Robert, Palo Alto, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002169307	A1	20021114

APPLICATION INFO.: US 2001-887540 A1 20010621 (9)

NUMBER DATE

PRIORITY INFORMATION: US 2000-213201P 20000621 (60)
US 2000-223123P 20000807 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DELTAGEN, INC., 1003 Hamilton Avenue, Menlo Park, CA, 94025
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 2105
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to transgenic animals, as well as compositions and methods relating to the characterization of gene function. Specifically, the present invention provides transgenic mice comprising mutations in a low density lipoprotein-related protein 5 gene. Such transgenic mice are useful as models for disease and for identifying agents that modulate gene expression and gene function, and as potential treatments for various disease states and disease conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 39 OF 45 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002219603 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11956231
TITLE: Cbfa1-independent decrease in osteoblast proliferation, osteopenia, and persistent embryonic eye vascularization in mice deficient in ***Lrp5*** , a Wnt coreceptor.
AUTHOR: Kato Masaki; Patel Millan S; Levasseur Regis; Lobov Ivan; Chang Benny H-J; Glass Donald A 2nd; Hartmann Christine; Li Lan; Hwang Tae-Ho; Brayton Cory F; Lang Richard A; Karsenty Gerard; Chan Lawrence
CORPORATE SOURCE: Department of Molecular and Cellular Biology and Medicine, Baylor College of Medicine, Houston, TX 77030, USA.
CONTRACT NUMBER: AR42919 (NIAMS)
DE11290 (NIDCR)
DK58882 (NIDDK)
HL16512 (NHLBI)
HL51586 (NHLBI)
SOURCE: Journal of cell biology, (2002 Apr 15) 157 (2) 303-14.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020417
Last Updated on STN: 20030105
Entered Medline: 20020516
AB The low-density lipoprotein receptor-related protein (Lrp)-5 functions as a Wnt coreceptor. Here we show that mice with a targeted disruption of ***Lrp5*** develop a low bone mass phenotype. In vivo and in vitro analyses indicate that this phenotype becomes evident postnatally, and demonstrate that it is secondary to decreased osteoblast proliferation and function in a Cbfa1-independent manner. ***Lrp5*** is expressed in ***osteoblasts*** and is required for optimal Wnt signaling in ***osteoblasts*** . In addition, ***Lrp5*** -deficient mice display persistent embryonic eye vascularization due to a failure of macrophage-induced endothelial cell apoptosis. These results implicate Wnt proteins in the postnatal control of vascular regression and bone formation, two functions affected in many diseases. Moreover, these features recapitulate human osteoporosis-pseudoglioma syndrome, caused by ***LRP5*** inactivation.

L5 ANSWER 40 OF 45 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:795757 CAPLUS
DOCUMENT NUMBER: 138:83661
TITLE: Insulin receptor substrate-2 maintains predominance of anabolic function over catabolic function of ***osteoblasts***
AUTHOR(S): Akune, Toru; Ogata, Naoshi; Hoshi, Kazuto; Kubota, Naoto; Terauchi, Yasuo; Tobe, Kazuyuki; Takagi, Hideko; Azuma, Yoshiaki; Kadowaki, Takashi; Nakamura, Kozo; Kawaguchi, Hiroshi
CORPORATE SOURCE: Department of Orthopaedic Surgery, University of Tokyo, Tokyo, 113-8655, Japan
SOURCE: Journal of Cell Biology (2002), 159(1), 147-156
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Insulin receptor substrates (IRS-1 and IRS-2) are essential for intracellular signaling by insulin and insulin-like growth factor-I (IGF-I), anabolic regulators of bone metab. Although mice lacking the IRS-2 gene (IRS-2-/- mice) developed normally, they exhibited osteopenia with decreased bone formation and increased bone resorption. Cultured

IRS-2-/- ***osteoblasts*** showed reduced differentiation and matrix
synthesis compared with wild-type ***osteoblasts*** . However, they
showed increased receptor activator of nuclear factor .kappa.B ligand
(RANKL) expression and osteoclastogenesis in the coculture with bone
marrow cells, which were restored by reintroduction of IRS-2 using an
adenovirus vector. Although IRS-2 was expressed and phosphorylated by
insulin and IGF-I in both ***osteoblasts*** and osteoclastic cells,
cultures in the absence of ***osteoblasts*** revealed that intrinsic
IRS-2 signaling in osteoclastic cells was not important for their
differentiation, function, or survival. It is concluded that IRS-2
deficiency in ***osteoblasts*** causes osteopenia through impaired
anabolic function and enhanced supporting ability of osteoclastogenesis.
We propose that IRS-2 is needed to maintain the predominance of bone
formation over bone resorption, whereas IRS-1 maintains bone turnover, as
we previously reported; the integration of these two signalings causes a
potent bone anabolic action by insulin and IGF-I.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 45 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001673198 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11719191
TITLE: ***LDL*** ***receptor*** - ***related*** ***protein*** ***5*** (***LRP5***) affects bone
accrual and eye development.
AUTHOR: Gong Y; Slee R B; Fukai N; Rawadi G; Roman-Roman S;
Reginato A M; Wang H; Cundy T; Glorieux F H; Lev D;
Zacharin M; Oexle K; Marcelino J; Suwairi W; Heeger S;
Sabatakos G; Apte S; Adkins W N; Allgrove J;
Arslan-Kirchner M; Batch J A; Beighton P; Black G C; Boles
R G; Boon L M; Borrone C; Brunner H G; Carle G F;
Dallapiccola B; De Paepe A; Floege B; Halfhide M L; Hall B;
Hennekam R C; Hirose T; Jans A; Juppner H; Kim C A;
Keppler-Noreuil K; Kohlschuetter A; LaCombe D; Lambert M;
Lemyre E; Letteboer T; Peltonen L; Ramesar R S; Romanengo
M; Somer H; Steichen-Gersdorf E; Steinmann B; Sullivan B;
Superti-Furga A; Swoboda W; van den Boogaard M J; Van Hul
W; Vikkula M; Votruba M; Zabel B; Garcia T; Baron R; Olsen
B R; Warman M L
CORPORATE SOURCE: Osteoporosis-Pseudoglioma Syndrome Collaborative Group.
SOURCE: Cell, (2001 Nov 16) 107 (4) 513-23.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011126
Last Updated on STN: 20030403
Entered Medline: 20020108
AB In humans, low peak bone mass is a significant risk factor for
osteoporosis. We report that ***LRP5*** , encoding the low-density
lipoprotein receptor-related protein 5, affects bone mass accrual during
growth. Mutations in ***LRP5*** cause the autosomal recessive
disorder osteoporosis-pseudoglioma syndrome (OPPG). We find that OPPG
carriers have reduced bone mass when compared to age- and gender-matched
controls. We demonstrate ***LRP5*** expression by ***osteoblasts***
in situ and show that ***LRP5*** can transduce Wnt signaling in vitro
via the canonical pathway. We further show that a mutant-secreted form of
LRP5 can reduce bone thickness in mouse calvarial explant
cultures. These data indicate that Wnt-mediated signaling via
LRP5 affects bone accrual during growth and is important for the
establishment of peak bone mass.

L5 ANSWER 42 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 2001:546888 BIOSIS
DOCUMENT NUMBER: PREV200100546888
TITLE: Human bone mass accrual is affected by mutations in the low
density lipoprotein receptor-related protein 5 gene (***LRP5***).
AUTHOR(S): Gong, Y. [Reprint author]; Slee, R. [Reprint author];
Osteoporosis-Pseudoglioma Collaborative Group
CORPORATE SOURCE: Department of Genetics and Center for Human Genetics, Case
Western Reserve University School of Medicine and
University Hospitals of Cleveland, Cleveland, OH, USA
SOURCE: American Journal of Human Genetics, (October, 2001) Vol.
69, No. 4 Supplement, pp. 189. print.
Meeting Info.: 51st Annual Meeting of the American Society
of Human Genetics. San Diego, California, USA. October
12-16, 2001.

CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002

L5 ANSWER 43 OF 45 MEDLINE on STN
DUPLICATE 9
ACCESSION NUMBER: 1999008902 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9790987
TITLE: Molecular cloning and characterization of ***LR3*** , a
novel LDL receptor family protein with mitogenic activity.
AUTHOR: Dong Y; Lathrop W; Weaver D; Qiu Q; Cini J; Bertolini D;
Chen D
CORPORATE SOURCE: Pharmaceutical Division, Bayer Corporation, West Haven,
Connecticut, 06516-4175, USA.
SOURCE: Biochemical and biophysical research communications, (1998
Oct 29) 251 (3) 784-90.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF077820
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981203
AB We report molecular cloning and initial functional characterization of a
novel member of the low density lipoprotein receptor (LDLR) gene family.
The cDNA was isolated from a human osteoblast cDNA library and encoded a
1,615 amino acids protein designated as ***LR3*** . It has, in the
extracellular region, a cluster of three LDLR ligand binding repeats at a
juxtamembrane position and four EGF precursor homology domains separated
by YWTD spacer repeats. The entire ectodomain shares the same modular
organization with the middle portion of the extracellular regions of two
LDLR family members, LDLR-related protein (LRP), and gp330/megalin.
LR3 mRNA was expressed in most of the adult and fetal tissues
examined. The highest expression level was seen in aorta. In human
osteosarcoma cells examined, ***LR3*** mRNA was highly enriched in
TE85 cells, moderately expressed in MG63 cells and primary human
osteoblasts , and undetectable in SaOS-2 cells. NIH 3T3 cells
transfected with either full length ***LR3*** or its ectodomain showed
significantly increased proliferation, whereas transfection of
intracellular domain had no proliferative effect. We predict that
LR3 is a multi-functional protein with potential mitogenic
activity.
Copyright 1998 Academic Press.

L5 ANSWER 44 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 1999:463 BIOSIS
DOCUMENT NUMBER: PREV199900000463
TITLE: Molecular cloning and characterization of ***LR3*** , a
novel LDL receptor family protein with mitogenic activity.
AUTHOR(S): Dong, Yu; Lathrop, William; Weaver, Daniel; Qiu, Qingqing;
Cini, John; Bertolini, Donald; Chen, David
CORPORATE SOURCE: Bayer Res. Cent., Pharmaceutical Div., Bayer Corporation,
400 Morgan Lane, West Haven, CT 06516-4175, USA
SOURCE: Biochemical and Biophysical Research Communications, (Oct.
29, 1998) Vol. 25, No. 3, pp. 784-790. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jan 1999
Last Updated on STN: 11 Jan 1999
AB We report molecular cloning and initial functional characterization of a
novel member of the low density lipoprotein receptor (LDLR) gene family.
The cDNA was isolated from a human osteoblast cDNA library and encoded a
1,615 amino acids protein designated as ***LR3*** . It has, in the
extracellular region, a cluster of three LDLR ligand binding repeats at a
juxtamembrane position and four EGF precursor homology domains separated
by YWTD spacer repeats. The entire ectodomain shares the same modular
organization with the middle portion of the extracellular regions of two
LDLR family members, LDLR-related protein (LRP), and gp330/megalin.
LR3 mRNA was expressed in most of the adult and fetal tissues
examined. The highest expression level was seen in aorta. In human
osteosarcoma cells examined, ***LR3*** mRNA was highly enriched in
TE85 cells, moderately expressed in MG63 cells and primary human
osteoblasts , and undetectable in SaOS-2 cells. NIH 3T3 cells
transfected with either full length ***LR3*** or its ectodomain showed
significantly increased proliferation, whereas transfection of
intracellular domain had no proliferative effect. We predict that
LR3 is a multifunctional protein with potential mitogenic
activity.

L5 ANSWER 45 OF 45 USPATFULL on STN
ACCESSION NUMBER: 97:109875 USPATFULL

TITLE: Endothelin antagonistic peptide derivatives
INVENTOR(S): Ishikawa, Kiyofumi, Tokyo, Japan
Fukami, Takehiro, Tokyo, Japan
Hayama, Takashi, Tokyo, Japan
Niiyama, Kenji, Tokyo, Japan
Nagase, Toshio, Tokyo, Japan
Mase, Toshiaki, Tokyo, Japan
Fujita, Kagari, Tokyo, Japan
Ihara, Masaki, Tokyo, Japan
Ikemoto, Fumihiko, Tokyo, Japan
Yano, Mitsuo, Tokyo, Japan
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5691315		19971125
APPLICATION INFO.:	US 1995-494818		19950626 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-213829, filed on 14 Mar 1994, now patented, Pat. No. US 5470833 which is a continuation of Ser. No. US 1992-884189, filed on 18 May 1992, now abandoned which is a division of Ser. No. US 1991-712095, filed on 7 Jun 1991, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-149105	19900607

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tsang, Cecilia J.
ASSISTANT EXAMINER: Marshall, S. G.
LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 5461
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to compounds which are antagonists of endothelin, to processes for their preparation, and to their use as pharmaceuticals.

The compounds of the invention are Useful in the treatment of hypertension, pulmonary hypertension, Reynaud's disease, myocardial infarction, angina pectoris, acute renal failure, cerebral infarction, cerebral vasospasm, arteriosclerosis, asthma, endotoxin shock, endotoxin-induced multiple organ failure or disseminated intravascular coagulation, and/or cyclosporin-induced renal failure or hypertension.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L6 120 L1 AND L3

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, BIOTECHNO, USPATFULL'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L6
L7 68 DUPLICATE REMOVE L6 (52 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 68 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 68 MEDLINE on STN
DUPLICATE 1
ACCESSION NUMBER: 2004616725 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15576404
TITLE: Sequential roles of Hedgehog and Wnt signaling in osteoblast development.
AUTHOR: Hu Hongliang; Hilton Matthew J; Tu Xiaolin; Yu Kai; Ornitz David M; Long Fanxin
CORPORATE SOURCE: Department of Medicine, Washington University Medical School, St. Louis, MO 63110, USA.
CONTRACT NUMBER: 5T32AR07033 (NIAMS)
DK065789 (NIDDK)
HD39952 (NICHD)
SOURCE: Development (Cambridge, England), (2005 Jan) 132 (1) 49-60.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050204
AB Signals that govern development of the osteoblast lineage are not well understood. Indian hedgehog (Ihh), a member of the hedgehog (Hh) family of proteins, is essential for osteogenesis in the endochondral skeleton during embryogenesis. The canonical pathway of Wnt signaling has been implicated by studies of ***Lrp5*** , a co-receptor for ***Wnt*** ***proteins*** , in postnatal bone mass homeostasis. In the present study we demonstrate that beta-catenin, a central player in the canonical Wnt pathway, is indispensable for osteoblast differentiation in the mouse embryo. Moreover, we present evidence that Wnt signaling functions downstream of Ihh in development of the osteoblast lineage. Finally Wnt7b is identified as a potential endogenous ligand regulating osteogenesis. These data support a model that integrates Hh and Wnt signaling in the regulation of osteoblast development.

L7 ANSWER 2 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:309387 USPATFULL
TITLE: Transgenic animal model of bone mass modulation
INVENTOR(S): Askew, G. Roger, Boxford, MA, UNITED STATES
Babij, Philip, Dunstable, MA, UNITED STATES
Bex, Frederick James, III, Newtown Square, PA, UNITED STATES
Nest Bodine, Peter Van, Havertown, PA, UNITED STATES
PATENT ASSIGNEE(S): Wyeth, Madison, NJ, UNITED STATES, 07940 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004244069	A1	20041202
APPLICATION INFO.:	US 2003-680287	A1	20031008 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2002-US14876, filed on 13 May 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-290071P	20010511 (60)
	US 2001-291311P	20010517 (60)
	US 2002-353058P	20020201 (60)
	US 2002-361293P	20020304 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 44
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 61 Drawing Page(s)
LINE COUNT: 8213
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to express the HBM protein in animal cells and transgenic animals. The present invention also relates to transgenic animals expressing the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The invention provides nucleic acids, including coding sequences, oligonucleotide primers and probes, proteins, cloning vectors, expression vectors, transformed hosts, methods of developing pharmaceutical compositions, methods of identifying molecules involved in bone development, and methods of diagnosing and treating diseases involved in bone development. In preferred embodiments, the present invention is directed to methods for treating, diagnosing and preventing osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:286719 USPATFULL
TITLE: Systems and methods for screening for modulators of neural differentiation
INVENTOR(S): Jessel, Thomas, Bronx, NY, UNITED STATES
Wichterle, Hynek, New York, NY, UNITED STATES
Wilson, Sara I., New York, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004224887	A1	20041111
APPLICATION INFO.:	US 2004-789308	A1	20040226 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-196882, filed on 16 Jul 2002, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Leslie Gladstone Restaino, Esq., Brown Raysman Millstein Felder & Steiner LLP, 163 Madison Avenue, P.O. Box 1989, Morristown, NJ, 07962-1989
NUMBER OF CLAIMS: 80
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 4179
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides in vitro systems for use in identifying modulators of neural differentiation. Also provided are modulators identified by these systems. The present invention further provides methods for identifying a modulator of neural differentiation, a modulator of a Wnt signalling pathway, a modulator of Wnt-dependent neural differentiation, a modulator of a BMP signalling pathway, a modulator of BMP-dependent neural differentiation, a modulator of a Hh signalling pathway, and a modulator of Hh-dependent neural differentiation. Also provided are modulators identified by these methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:286140 USPATFULL
TITLE: Systems and methods for screening for modulators of neural differentiation
INVENTOR(S): Jessel, Thomas, Bronx, NY, UNITED STATES
Wichterle, Hynek, New York, NY, UNITED STATES
Wilson, Sara, New York, NY, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2004224302 A1 20041111
APPLICATION INFO.: US 2004-789266 A1 20040226 (10)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-196882, filed on 16 Jul 2002, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Leslie Gladstone Restaino, Esq., Brown Raysman Millstein Felder & Steiner LLP, 163 Madison Avenue, P.O. Box 1989, Morristown, NJ, 07962-1989
NUMBER OF CLAIMS: 67
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 4051
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides in vitro systems for use in identifying modulators of neural differentiation. Also provided are modulators identified by these systems. The present invention further provides methods for identifying a modulator of neural differentiation, a modulator of an FGF signalling pathway, a modulator of FGF-dependent neural differentiation, a modulator of a retinoid signalling pathway, and a modulator of retinoid-dependent neural differentiation. Also provided are modulators identified by these methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:282022 USPATFULL
TITLE: Transgenic animal model of bone mass modulation
INVENTOR(S): Babij, Philip, Newbury Park, CA, UNITED STATES
Bex, Frederick James, Newton Square, PA, UNITED STATES
Bodine, Peter Van Nest, Havertown, PA, UNITED STATES
Askew, G. Roger, Boxford, MA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2004221326 A1 20041104
APPLICATION INFO.: US 2004-477238 A1 20040412 (10)
WO 2002-US14876 20020513

NUMBER DATE

PRIORITY INFORMATION: US 2001-60290071 20010511
US 2001-60291311 20010517
US 2002-60353058 20020201
US 2002-60361293 20020304
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 61 Drawing Page(s)
LINE COUNT: 7878
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and materials used to express the HBM protein in animal cells and transgenic animals. The present invention also relates to transgenic animals expressing the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The invention provides nucleic acids, including coding sequences, oligonucleotide primers and probes, proteins, cloning vectors, expression vectors, transformed hosts, methods of developing pharmaceutical compositions, methods of identifying molecules involved in bone development, and methods of diagnosing and treating diseases involved in bone development. In preferred embodiments, the present invention is directed to methods for treating, diagnosing and preventing osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:221788 USPATFULL
TITLE: Protection of stem cells from cytotoxic agents by modulation of beta-catenin signaling pathways
INVENTOR(S): Weissman, Irving, Redwood City, CA, UNITED STATES
Reya, Tannishtha, Chapel Hill, NC, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2004171559 A1 20040902
APPLICATION INFO.: US 2003-729548 A1 20031205 (10)

NUMBER DATE

PRIORITY INFORMATION: US 2002-431655P 20021206 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO PARK, CA, 94025
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 1784
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Reagents that block the extracellular activation of .beta.-catenin are
used to induce quiescence in normal stem cells, in order to reduce the
killing of stem cells by anti-proliferative agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:51429 USPATFULL
TITLE: Reagents and methods for modulating dkk-mediated
interactions
INVENTOR(S): Allen, Kristina M., Hopkinton, MA, UNITED STATES
Anisowicz, Anthony, West Newton, MA, UNITED STATES
Damagnez, Veronique, Framingham, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004038860	A1	20040226
APPLICATION INFO.:	US 2002-182936	A1	20020802 (10)
	WO 2002-US15982		20020517

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 114
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Page(s)
LINE COUNT: 5224
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides reagents, compounds, compositions, and
methods relating to novel interactions of the extracellular domain of
LRP5 , HBM (a variant of ***LRP5***), and/or LRP6 with Dkk,
including Dkk-1. The various nucleic acids, polypeptides, antibodies,
assay methods, diagnostic methods, and methods of treatment of the
present invention are related to and impact on Dkk, ***LRP5*** ,
LRP6, HBM, and Wnt signaling. Dkk, ***LRP5*** , LRP6, HBM, and Wnt
are implicated in bone and lipid cellular signaling. Thus, the present
invention provides reagents and methods for modulating lipid levels
and/or bone mass and is useful in the treatment and diagnosis of
abnormal lipid levels and bone mass disorders, such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:44501 USPATFULL
TITLE: Proteins and nucleic acids encoding same
INVENTOR(S): Tchernev, Velizar T., Branford, CT, UNITED STATES
Spytek, Kimberly A., New Haven, CT, UNITED STATES
Zerhusen, Bryan D., Branford, CT, UNITED STATES
Patturajan, Meera, Branford, CT, UNITED STATES
Shimkets, Richard A., West Haven, CT, UNITED STATES
Li, Li, Branford, CT, UNITED STATES
Gangolli, Esha A., Madison, CT, UNITED STATES
Padigaru, Muralidhara, Branford, CT, UNITED STATES
Anderson, David W., Branford, CT, UNITED STATES
Rastelli, Luca, Guilford, CT, UNITED STATES
Miller, Charles E., Hill Drive, CT, UNITED STATES
Gerlach, Valerie, Branford, CT, UNITED STATES
Taupier, Raymond J., JR., East Haven, CT, UNITED STATES
Gusev, Vladimir Y., UNITED STATES
Colman, Steven D., Guilford, CT, UNITED STATES
Wolenc, Adam Ryan, New Haven, CT, UNITED STATES
Pena, Carol E. A., Guilford, CT, UNITED STATES
Furtak, Katarzyna, Anosia, CT, UNITED STATES
Grosse, William M., Bransford, CT, UNITED STATES
Alsobrook, John P., II, Madison, CT, UNITED STATES
Lepley, Denise M., Branford, CT, UNITED STATES
Rieger, Daniel K., Branford, CT, UNITED STATES
Burgess, Catherine E., Wethersfield, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004033493	A1	20040219
APPLICATION INFO.:	US 2002-72012	A1	20020131 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-267459P	20010208 (60)
	US 2001-266975P	20010207 (60)
	US 2001-267057P	20010207 (60)
	US 2001-266767P	20010205 (60)
	US 2001-266406P	20010202 (60)
	US 2001-265395P	20010131 (60)
	US 2001-265412P	20010131 (60)
	US 2001-265517P	20010131 (60)
	US 2001-265514P	20010131 (60)
	US 2001-267823P	20010209 (60)
	US 2001-268974P	20010215 (60)
	US 2001-271855P	20010227 (60)
	US 2001-271839P	20010227 (60)
	US 2001-273046P	20010302 (60)
	US 2001-272788P	20010302 (60)
	US 2001-275989P	20010314 (60)
	US 2001-275925P	20010314 (60)
	US 2001-275947P	20010314 (60)
	US 2001-275950P	20010314 (60)

US 2001-276450P 20010315 (60)
US 2001-276448P 20010315 (60)
US 2001-276397P 20010316 (60)
US 2001-276768P 20010316 (60)
US 2001-278652P 20010320 (60)
US 2001-278775P 20010326 (60)
US 2001-278778P 20010326 (60)
US 2001-279882P 20010329 (60)
US 2001-279884P 20010329 (60)
US 2001-280147P 20010330 (60)
US 2001-283083P 20010411 (60)
US 2001-282992P 20010411 (60)
US 2001-285133P 20010420 (60)
US 2001-285749P 20010423 (60)
US 2001-288327P 20010503 (60)
US 2001-288504P 20010503 (60)
US 2001-294047P 20010529 (60)
US 2001-294473P 20010530 (60)
US 2001-296964P 20010608 (60)
US 2001-298959P 20010618 (60)
US 2001-299324P 20010619 (60)
US 2001-312020P 20010813 (60)
US 2001-312908P 20010816 (60)
US 2001-312889P 20010816 (60)
US 2001-313930P 20010821 (60)
US 2001-315470P 20010828 (60)
US 2001-316447P 20010831 (60)
US 2001-318115P 20010907 (60)
US 2001-318118P 20010907 (60)
US 2001-318740P 20010912 (60)
US 2001-323379P 20010919 (60)
US 2001-330308P 20011018 (60)
US 2001-330245P 20011018 (60)
US 2001-332701P 20011114 (60)
US 2001-271664P 20010226 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Ivor R. Elrifi, Ph.D., Mintz, Levin, Cohn, Ferris,, Glovsky and Popeo, P.C., One Financial Center, Boston, MA, 02111
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
LINE COUNT: 59681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein are nucleic acid sequences that encode novel polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:31217 USPATFULL
TITLE: Wise/Sost nucleic acid sequences and amino acid sequences
INVENTOR(S): Krumlauf, Robb, Mission Hills, KS, UNITED STATES
Ellies, Debra, Kansas City, MO, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004023356	A1	20040205
APPLICATION INFO.:	US 2003-464368	A1	20030616 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-388970P	20020614 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: POLSINELLI SHALTON & WELTE, P.C., Suite 1000, 700 W. 47th Street, Kansas City, MO, 64108
NUMBER OF CLAIMS: 235
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 4672
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to nucleic acid sequences and amino acid sequences which influence bone deposition, the Wnt pathway, ocular development, tooth development, and may bind to LRP. The nucleic acid sequence and polypeptides include Wise and Sost as well as a family of molecules which express a cysteine knot polypeptide. Additionally, the present invention relates to various molecular tools derived from the nucleic acids and polypeptides including vectors, transfected host cells, monochronal antibodies, Fab fragments, and methods for impacting the pathways.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:18907 USPATFULL
TITLE: Compositions and methods for modulating cell differentiation
INVENTOR(S): Lassar, Andrew B., Newton Center, MA, UNITED STATES
Mercola, Mark, Del Mar, CA, UNITED STATES
Gupta, Ruchika, San Diego, CA, UNITED STATES
Marvin, Martha, Brookline, MA, UNITED STATES
Schneider, Valerie, Philadelphia, PA, UNITED STATES
Tzahor, Eldad, Brookline, MA, UNITED STATES
Brott, Barbara, Boston, MA, UNITED STATES
Sokol, Sergei, Boston, MA, UNITED STATES

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2004014209 A1 20040122
APPLICATION INFO.: US 2003-351275 A1 20030123 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-351126P	20020123 (60)
	US 2002-352456P	20020128 (60)
	US 2002-352665P	20020129 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FOLEY HOAG, LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BLVD, BOSTON, MA, 02110
NUMBER OF CLAIMS: 61
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 24 Drawing Page(s)
LINE COUNT: 4008
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compositions and methods for stimulating differentiation of stem cells into cardiac cells. The methods of the invention involve contacting a population cells comprising stem cells with at least one Wnt antagonist, such as a polypeptide or polypeptide fragment. In certain embodiments, the methods of the invention involve ***Dkk*** ***proteins*** or fragments, homologs, derivatives, variants, or peptidomimetics thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 11 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2004:13003 USPATFULL
TITLE: Diagnosis, prognosis and identification of potential therapeutic targets of multiple myeloma based on gene expression profiling
INVENTOR(S): Shaughnessy, John D., Little Rock, AR, UNITED STATES
Zhan, Fenghuang, Little Rock, AR, UNITED STATES
Barlogie, Bart, Little Rock, AR, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004009523	A1	20040115
APPLICATION INFO.:	US 2003-454263	A1	20030604 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-409004, filed on 8 Apr 2003, PENDING Continuation-in-part of Ser. No. US 2002-289746, filed on 7 Nov 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-403075P	20020813 (60)
	US 2001-348238P	20011107 (60)
	US 2002-355386P	20020208 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 24 Drawing Page(s)
LINE COUNT: 4510
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gene expression profiling between normal B cells/plasma cells and multiple myeloma cells revealed four distinct subgroups of multiple myeloma plasma cells that have significant correlation with clinical characteristics known to be associated with poor prognosis. Diagnosis for multiple myeloma (and possibly monoclonal gammopathy of undetermined significance) based on differential expression of 14 genes, as well as prognostics for the four subgroups of multiple myeloma based on the expression of 24 genes were also established. Gene expression profiling also allows placing multiple myeloma into a developmental schema parallel to that of normal plasma cell differentiation. The development of a gene expression- or developmental stage-based classification system for multiple myeloma would lead to rational design of more accurate and sensitive diagnostics, prognostics and tumor-specific therapies for multiple myeloma.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 12 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004243930 EMBASE
TITLE: Multiple mechanisms for Wnt11-mediated repression of the canonical Wnt signaling pathway.
AUTHOR: Maye P.; Zheng J.; Li L.; Wu D.
CORPORATE SOURCE: D. Wu, Dept. of Genet. and Devmtl. Biology, Univ. of Connecticut Health Center, MC3301, 263 Farmington Ave., Farmington, CT 06030, United States. dwu@neuron.uchc.edu
SOURCE: Journal of Biological Chemistry, (4 Jun 2004) 279/23 (24659-24665).
Refs: 48
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The effect of a noncanonical Wnt, Wnt11, on canonical Wnt signaling stimulated by Wnt1 and activated forms of ***LRP5*** (low density

lipoprotein receptor-related protein-5), Dishevelled1 (Dvl1), and
.beta.-catenin was examined in NIH3T3 cells and P19 embryonic carcinoma
cells. Wnt11 repressed Wnt1-mediated activation of LEF-1 reporter activity
in both cell lines. However, Wnt11 was unable to inhibit canonical
signaling activated by ***LRP5*** , Dvl1, or .beta.-catenin in NIH3T3
cells, although it could in P19 cells. In addition, Wnt11-mediated
inhibition of canonical signaling in NIH3T3 cells is ligand-specific;
Wnt11 could effectively repress canonical signaling activated by Wnt1,
Wnt3, or Wnt3a but not by Wnt7a or Wnt7b. Co-culture experiments with
NIH3T3 cells showed that the co-expression of Wnt11 with Wnt1 was not an
essential requirement for the inhibition, suggesting receptor competition
as a possible mechanism. Moreover, in both cell types, elevation of
intracellular Ca(2+) levels, which can result from Wnt11 treatment, led to
the inhibition of canonical signaling. This result suggests that Wnt11
might not be able to signal in NIH3T3. Furthermore, P19 cells were found
to express both endogenous canonical Wnts and Wnt11. Knockdown of Wnt11
expression using siRNA resulted in increased LEF-1 reporter activity, thus
indicating that Wnt11-mediated suppression of canonical signaling exists
in vivo.

L7 ANSWER 13 OF 68 MEDLINE on STN
DUPLICATE 2
ACCESSION NUMBER: 2004197066 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14739301
TITLE: The low density lipoprotein receptor-1, LRP1, interacts
with the human frizzled-1 (HFz1) and down-regulates the
canonical Wnt signaling pathway.
AUTHOR: Zilberberg Alona; Yaniv Abraham; Gazit Arnona
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of
Medicine, Tel Aviv University, Tel Aviv 69978, Israel.
SOURCE: Journal of biological chemistry, (2004 Apr 23) 279 (17)
17535-42.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040420
Last Updated on STN: 20040611
Entered Medline: 20040610
AB Members of the low density lipoprotein receptor family (LDLR),
LRP5 /6, were shown to interact with the Frizzled (Fz) receptors
and to function as Wnt coreceptors. Here we show that mLRP4T100, a
minireceptor of LRP1, another member of the LDLR family, interacts with
the human Fz-1 (HFz1), previously shown to serve as a receptor
transmitting the canonical Wnt-3a-induced signaling cascade. However, in
contrast to ***LRP5*** /6, mLRP4T100, as well as the full-length LRP1,
did not cooperate with HFz1 in transmitting the Wnt-3a signaling but
rather repressed it. mLRP4T100 inhibitory effect was displayed also by
endocytosis-defective mLRP4T100 mutants, suggesting that LRP1 repressive
effect is not attributable to LRP1-mediated enhanced HFz1 internalization
and subsequent degradation. Enforced expression of mLRP4T100 decreased
the capacity of HFz1 cysteine-rich domain (CRD) to interact with LRP6, in
contrast to HFz1-CRD/Wnt-3a interaction that was not disrupted by
overexpressing mLRP4T100. These data suggest that LRP1, by sequestering
HFz1, disrupts the receptor/coreceptor complex formation, leading to the
repression of the canonical Wnt signaling. Thus, this study implies that
the ability to interact with Fz receptors is shared by several members of
the LDLR family. However, whereas some members of the LDLR family, such
as ***LRP5*** /6, interact with Fz and serve as Wnt coreceptors, others
negatively regulate Wnt signaling, presumably by sequestering Fz.

L7 ANSWER 14 OF 68 MEDLINE on STN
DUPLICATE 3
ACCESSION NUMBER: 2004562796 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15459103
TITLE: Wnt signals across the plasma membrane to activate the
beta-catenin pathway by forming oligomers containing its
receptors, Frizzled and LRP.
AUTHOR: Cong Feng; Schweizer Liang; Varmus Harold
CORPORATE SOURCE: Cancer Biology and Genetics Program, Sloan-Kettering
Institute, Memorial Sloan-Kettering Cancer Center, New
York, NY 10021, USA.. feng.cong@pharma.novartis.com
SOURCE: Development (Cambridge, England), (2004 Oct) 131 (20)
5103-15.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041111
Last Updated on STN: 20041229

Entered Medline: 20041228

AB Wnt-induced signaling via beta-catenin plays crucial roles in animal development and tumorigenesis. Both a seven-transmembrane protein in the Frizzled family and a single transmembrane protein in the LRP family (***LDL*** - ***receptor*** - ***related*** ***protein*** ***5*** /6 or Arrow) are essential for efficiently transducing a signal from Wnt, an extracellular ligand, to an intracellular pathway that stabilizes beta-catenin by interfering with its rate of destruction. However, the molecular mechanism by which these two types of membrane receptors synergize to transmit the Wnt signal is not known. We have used mutant and chimeric forms of Frizzled, LRP and ***Wnt*** ***proteins*** , small inhibitory RNAs, and assays for beta-catenin-mediated signaling and protein localization in Drosophila S2 cells and mammalian 293 cells to study transmission of a Wnt signal across the plasma membrane. Our findings are consistent with a mechanism by which ***Wnt*** ***protein*** binds to the extracellular domains of both LRP and Frizzled receptors, forming membrane-associated hetero-oligomers that interact with both Disheveled (via the intracellular portions of Frizzled) and Axin (via the intracellular domain of LRP). This model takes into account several observations reported here: the identification of intracellular residues of Frizzled required for beta-catenin signaling and for recruitment of Dvl to the plasma membrane; evidence that Wnt3A binds to the ectodomains of LRP and Frizzled; and demonstrations that a requirement for Wnt ligand can be abrogated by chimeric receptors that allow formation of Frizzled-LRP hetero-oligomers. In addition, the beta-catenin signaling mediated by ectopic expression of LRP is not dependent on Disheveled or Wnt, but can also be augmented by oligomerization of LRP receptors.

L7 ANSWER 15 OF 68 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2004306948 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15064719

TITLE: Truncated mutants of the putative Wnt receptor LRP6/Arrow can stabilize beta-catenin independently of Frizzled proteins.

AUTHOR: Brennan Keith; Gonzalez-Sancho Jose M; Castelo-Soccio Leslie A; Howe Louise R; Brown Anthony M C

CORPORATE SOURCE: Strang Cancer Research Laboratory at The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.

CONTRACT NUMBER: CA47207 (NCI) GM67739 (NIGMS)

SOURCE: Oncogene, (2004 Jun 17) 23 (28) 4873-84.

Journal code: 8711562. ISSN: 0950-9232.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200407

ENTRY DATE: Entered STN: 20040624
Last Updated on STN: 20040717
Entered Medline: 20040716

AB Secreted signaling proteins of the Wnt family are known to regulate a diverse range of developmental processes, and their signaling pathway through beta-catenin is frequently activated in cancer. The identification of both Frizzled and ***LRP5*** /6 (LRP: low-density lipoprotein receptor-related protein) proteins as components of cell-surface receptors for ***Wnt*** ***proteins*** has raised questions about their individual functions. We have investigated this issue through a structure-function analysis of Frizzled and LRP proteins that have been implicated in Wnt1 signaling. Consistent with other reports, we find that LRP6/Arrow proteins deleted for their extracellular domain are able to activate the Wnt/beta-catenin signaling pathway. Importantly, our results demonstrate that this signaling from LRP6/Arrow derivatives can occur in a Frizzled- and ligand-independent manner. Furthermore, we show that the PPSP motifs within the intracellular domain of LRP6 are required for signaling. In contrast to results with LRP6, overexpression of Frizzled proteins did not activate the pathway. Based on evidence of ligand binding to both Frizzled and LRP6, current models suggest that both proteins are components of a Wnt receptor complex that signals to beta-catenin. In light of these models, our data imply that ***LRP5*** /6/Arrow proteins constitute the distal signal-initiating component of these receptors. The results also support the notion that ***LRP5*** /6 are candidate oncogenes.

L7 ANSWER 16 OF 68 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 2004263880 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15143170

TITLE: ***Wnt*** ***proteins*** induce dishevelled phosphorylation via an ***LRP5*** /6-independent

mechanism, irrespective of their ability to stabilize
beta-catenin.
AUTHOR: Gonzalez-Sancho Jose M; Brennan Keith R; Castelo-Soccio
Leslie A; Brown Anthony M C
CORPORATE SOURCE: Strang Cancer Research Laboratory at The Rockefeller
University, 1230 York Ave., New York, NY 10021, USA.
CONTRACT NUMBER: CA47207 (NCI)
GM67739 (NIGMS)
SOURCE: Molecular and cellular biology, (2004 Jun) 24 (11) 4757-68.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040528
Last Updated on STN: 20040624
Entered Medline: 20040621
AB Wnt glycoproteins play essential roles in the development of metazoan
organisms. Many ***Wnt*** ***proteins*** , such as Wnt1, activate
the well-conserved canonical Wnt signaling pathway, which results in
accumulation of beta-catenin in the cytosol and nucleus. Other Wnts, such
as Wnt5a, activate signaling mechanisms which do not involve beta-catenin
and are less well characterized. Dishevelled (Dvl) is a key component of
Wnt/beta-catenin signaling and becomes phosphorylated upon activation of
this pathway. In addition to Wnt1, we show that several ***Wnt***
proteins , including Wnt5a, trigger phosphorylation of mammalian
Dvl proteins and that this occurs within 20 to 30 min. Unlike the effects
of Wnt1, phosphorylation of Dvl in response to Wnt5a is not concomitant
with beta-catenin stabilization, indicating that Dvl phosphorylation is
not sufficient to activate canonical Wnt/beta-catenin signaling.
Moreover, neither Dickkopf1, which inhibits Wnt/beta-catenin signaling by
binding the Wnt coreceptors ***LRP5*** and -6, nor dominant-negative
LRP5 /6 constructs could block Wnt-mediated Dvl phosphorylation.
We conclude that Wnt-induced phosphorylation of Dvl is independent of
LRP5 /6 receptors and that canonical Wnts can elicit both
LRP-dependent (to beta-catenin) and LRP-independent (to Dvl) signals. Our
data also present Dvl phosphorylation as a general biochemical assay for
Wnt ***protein*** function, including those Wnts that do not
activate the Wnt/beta-catenin pathway.

L7 ANSWER 17 OF 68 MEDLINE on STN
DUPLICATE 6
ACCESSION NUMBER: 2004244690 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15143163
TITLE: The ***LRP5*** high-bone-mass G171V mutation disrupts
LRP5 interaction with Mesd.
AUTHOR: Zhang Yazhou; Wang Yang; Li Xiaofeng; Zhang Jianhong; Mao
Junhao; Li Zhong; Zheng Jie; Li Lin; Harris Steve; Wu
Dianqing
CORPORATE SOURCE: Department of Genetics and Developmental Biology,
University of Connecticut Health Center, 263 Farmington
Ave., Farmington, CT 06410, USA.
CONTRACT NUMBER: CA85420 (NCI)
GM54167 (NIGMS)
SOURCE: Molecular and cellular biology, (2004 Jun) 24 (11) 4677-84.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040515
Last Updated on STN: 20040624
Entered Medline: 20040621
AB The mechanism by which the high-bone-mass (HBM) mutation (G171V) of the
Wnt coreceptor ***LRP5*** regulates canonical Wnt signaling was
investigated. The mutation was previously shown to reduce DKK1-mediated
antagonism, suggesting that the first YWTD repeat domain where G171 is
located may be responsible for DKK-mediated antagonism. However, we found
that the third YWTD repeat, but not the first repeat domain, is required
for DKK1-mediated antagonism. Instead, we found that the G171V mutation
disrupted the interaction of ***LRP5*** with Mesd, a chaperone protein
for ***LRP5*** /6 that is required for transport of the coreceptors to
cell surfaces, resulting in fewer ***LRP5*** molecules on the cell
surface. Although the reduction in the number of cell surface
LRP5 molecules led to a reduction in Wnt signaling in a paracrine
paradigm, the mutation did not appear to affect the activity of
coexpressed Wnt in an autocrine paradigm. Together with the observation
that osteoblast cells produce autocrine canonical Wnt, Wnt7b, and that
osteocytes produce paracrine DKK1, we think that the G171V mutation may
cause an increase in Wnt activity in osteoblasts by reducing the number of
targets for paracrine DKK1 to antagonize without affecting the activity of
autocrine Wnt.

L7 ANSWER 18 OF 68 MEDLINE on STN
DUPLICATE 7
ACCESSION NUMBER: 2004270551 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15142971
TITLE: The Wnt co-receptors ***Lrp5*** and Lrp6 are essential
for gastrulation in mice.
AUTHOR: Kelly Olivia G; Pinson Kathy I; Skarnes William C
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of
California at Berkeley, Berkeley, CA 94720-3200, USA.
SOURCE: Development (Cambridge, England), (2004 Jun) 131 (12)
2803-15.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040602
Last Updated on STN: 20040811
Entered Medline: 20040810
AB Recent work has identified LDL receptor-related family members,
Lrp5 and Lrp6, as co-receptors for the transduction of Wnt
signals. Our analysis of mice carrying mutations in both ***Lrp5***
and Lrp6 demonstrates that the functions of these genes are redundant and
are essential for gastrulation. ***Lrp5*** ;Lrp6 double homozygous
mutants fail to establish a primitive streak, although the anterior
visceral endoderm and anterior epiblast fates are specified. Thus,
Lrp5 and Lrp6 are required for posterior patterning of the
epiblast, consistent with a role in transducing Wnt signals in the early
embryo. Interestingly, ***Lrp5*** (+/-);Lrp6(-/-) embryos die shortly
after gastrulation and exhibit an accumulation of cells at the primitive
streak and a selective loss of paraxial mesoderm. A similar phenotype is
observed in Fgf8 and Fgfr1 mutant embryos and provides genetic evidence in
support of a molecular link between the Fgf and Wnt signaling pathways in
patterning nascent mesoderm. ***Lrp5*** (+/-);Lrp6(-/-) embryos also
display an expansion of anterior primitive streak derivatives and anterior
neurectoderm that correlates with increased Nodal expression in these
embryos. The effect of reducing, but not eliminating, Wnt signaling in
Lrp5 (+/-);Lrp6(-/-) mutant embryos provides important insight into
the interplay between Wnt, Fgf and Nodal signals in patterning the early
mouse embryo.

L7 ANSWER 19 OF 68 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2004190880 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15087387
TITLE: Dickkopf 3 inhibits invasion and motility of Saos-2
osteosarcoma cells by modulating the Wnt-beta-catenin
pathway.
AUTHOR: Hoang Bang H; Kubo Tadahiko; Healey John H; Yang Rui;
Nathan Saminathan S; Kolb E Anders; Mazza BethAnne; Meyers
Paul A; Gorlick Richard
CORPORATE SOURCE: Department of Surgery, Orthopaedic Surgery Service,
Memorial Sloan-Kettering Cancer Center, New York, New York,
USA.
CONTRACT NUMBER: CA-81832 (NCI)
SOURCE: Cancer research, (2004 Apr 15) 64 (8) 2734-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040417
Last Updated on STN: 20040611
Entered Medline: 20040610
AB Osteosarcoma (OS) is a primary malignancy of bone with a tendency to
metastasize early. Despite intensive chemotherapy and surgical resection,
approximately 30% of patients still develop distant metastasis. Our
previous work using clinical OS samples suggested that expression of the
Wnt receptor ***LRP5*** might be associated with tumor metastasis. In
the present study, we used a Dickkopf (Dkk) family member and a
dominant-negative ***LRP5*** receptor construct to modulate Wnt
signaling in OS cells. Saos-2 cells, which ectopically express Dkk-3, do
not undergo apoptosis and exhibit enhanced resistance to serum starvation
and chemotherapy-induced cytotoxicity. Transfection of Dkk-3 and
dominant-negative ***LRP5*** into Saos-2 cells significantly reduces
invasion capacity and cell motility. This blockade is associated with
changes in cell morphology consistent with a less invasive phenotype. In
addition, Dkk-3 and dominant-negative ***LRP5*** also induce changes
in beta-catenin localization consistent with an increase in cell-cell
adhesion. Taken together, these results support a possible role for Wnt
signaling in the pathobiology and progression of human OS.

L7 ANSWER 20 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004288152 EMBASE
TITLE: Hypomorphic expression of Dkk1 in the doublebridge mouse:

Dose dependence and compensatory interactions with Lrp6.
AUTHOR: MacDonald B.T.; Adamska M.; Meisler M.H.
CORPORATE SOURCE: M.H. Meisler, Department of Human Genetics, University of
Michigan, Ann Arbor, MI 48109-0618, United States.
meislerm@umich.edu
SOURCE: Development, (2004) 131/11 (2543-2552).
Refs: 48
ISSN: 0950-1991 CODEN: DEVPED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB doubleridge is a transgene-induced mouse mutation displaying forelimb
postaxial polysyndactyly. We have cloned the doubleridge transgene
insertion site and demonstrate that doubleridge acts in cis from a
distance of 150 kb to reduce the expression of dickkopf 1 (Dkk1), the
secreted Wnt antagonist. Expression of Dkk1 from the doubleridge allele
ranges from 35% of wild-type level in E7.0 head to <1% of wild type in
E13.5 tail. doubleridge homozygotes and doubleridge/null compound
heterozygotes are viable. An allelic series combining the wild-type,
doubleridge and null alleles of Dkk1 demonstrates the effect of varying
Dkk1 concentration on development of limb, head and vertebrae. Decreasing
expression of Dkk1 results in hemivertebral fusions in progressively more
anterior positions, with severity increasing from tail kinks to spinal
curvature. We demonstrated interaction between Dkk1 and the Wnt
co-receptors ***Lrp5*** and Lrp6 by analysis of several types of
double mutants. The polydactyly of Dkk1(d/d) mice was corrected by reduced
expression of ***Lrp5*** or Lrp6. The posterior digit loss and axial
truncation characteristic of Lrp6 null mice was partially corrected by
reduction of Dkk1. Similarly, the anterior head truncation characteristic
of Dkk1 null mice was rescued by reduction of Lrp6. These compensatory
interactions between Dkk1 and Lrp6 demonstrate the importance of correctly
balancing positive and negative regulation of Wnt signaling during
mammalian development.

L7 ANSWER 21 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004204271 EMBASE
TITLE: High-Bone-Mass Disease and ***LRP5*** [2] (multiple
letters).
AUTHOR: Whyte M.P.; Reinus W.H.; Mumm S.; Boyden L.M.; Insogna K.;
Lifton R.P.
CORPORATE SOURCE: Dr. M.P. Whyte, Washington Univ. School of Medicine, St.
Louis, MO 63110, United States
SOURCE: New England Journal of Medicine, (13 May 2004) 350/20
(2096-2099).
ISSN: 0028-4793 CODEN: NEJMAG
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
029 Clinical Biochemistry
033 Orthopedic Surgery
LANGUAGE: English

L7 ANSWER 22 OF 68 MEDLINE on STN
DUPLICATE 9
ACCESSION NUMBER: 2004225645 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15084453
TITLE: ***LDL*** ***receptor*** - ***related***
proteins ***5*** and 6 in Wnt/beta-catenin
signaling: arrows point the way.
AUTHOR: He Xi; Semenov Mikhail; Tamai Keiko; Zeng Xin
CORPORATE SOURCE: Division of Neuroscience, Children's Hospital, Harvard
Medical School, Boston, MA 02115, USA..
xi.he@childrens.harvard.edu
SOURCE: Development (Cambridge, England), (2004 Apr) 131 (8)
1663-77. Ref: 142
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040506
Last Updated on STN: 20040604
Entered Medline: 20040603
AB Wnt signaling through the canonical beta-catenin pathway plays essential
roles in development and disease. Low-density-lipoprotein
receptor-related proteins 5 and 6 (***Lrp5*** and Lrp6) in
vertebrates, and their Drosophila ortholog Arrow, are single-span
transmembrane proteins that are indispensable for Wnt/beta-catenin
signaling, and are likely to act as Wnt co-receptors. This review
highlights recent progress and unresolved issues in understanding the
function and regulation of Arrow/ ***Lrp5*** /Lrp6 in Wnt signaling. We
discuss Arrow/ ***Lrp5*** /Lrp6 interactions with Wnt and the Frizzled

family of Wnt receptors, and with the intracellular beta-catenin
degradation apparatus. We also discuss the regulation of ***Lrp5***
/Lrp6 by other extracellular ligands, and ***LRP5*** mutations
associated with familial osteoporosis and other disorders.

L7 ANSWER 23 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2004143155 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15035989
TITLE: Vascular development in the retina and inner ear: control
by Norrin and Frizzled-4, a high-affinity ligand-receptor
pair.
AUTHOR: Xu Qiang; Wang Yanshu; Dabdoub Alain; Smallwood Philip M;
Williams John; Woods Chad; Kelley Matthew W; Jiang Li;
Tasman William; Zhang Kang; Nathans Jeremy
CORPORATE SOURCE: Department of Molecular Biology and Genetics, Howard Hughes
Medical Institute, Johns Hopkins University School of
Medicine, Baltimore, MD 21205, USA.
SOURCE: Cell, (2004 Mar 19) 116 (6) 883-95.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040324
Last Updated on STN: 20040428
Entered Medline: 20040427
AB Incomplete retinal vascularization occurs in both Norrie disease and
familial exudative vitreoretinopathy (FEVR). Norrin, the protein product
of the Norrie disease gene, is a secreted protein of unknown biochemical
function. One form of FEVR is caused by defects in Frizzled-4 (Fz4), a
presumptive Wnt receptor. We show here that Norrin and Fz4 function as a
ligand-receptor pair based on (1) the similarity in vascular phenotypes
caused by Norrin and Fz4 mutations in humans and mice, (2) the specificity
and high affinity of Norrin-Fz4 binding, (3) the high efficiency with
which Norrin induces Fz4- and Lrp-dependent activation of the classical
Wnt pathway, and (4) the signaling defects displayed by disease-associated
variants of Norrin and Fz4. These data define a Norrin-Fz4 signaling
system that plays a central role in vascular development in the eye and
ear, and they indicate that ligands unrelated to Wnts can act through Fz
receptors.

L7 ANSWER 24 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004148103 EMBASE
TITLE: Mutations in ***LRP5*** or FZD4 Underlie the Common
Familial Exudative Vitreoretinopathy Locus on Chromosome
11q.
AUTHOR: Toomes C.; Bottomley H.M.; Jackson R.M.; Towns K.V.; Scott
S.; Mackey D.A.; Craig J.E.; Jiang L.; Yang Z.; Trembath
R.; Woodruff G.; Gregory-Evans C.Y.; Gregory-Evans K.;
Parker M.J.; Black G.C.M.; Downey L.M.; Zhang K.;
Inglehearn C.F.
CORPORATE SOURCE: Dr. C. Toomes, Molecular Medicine Unit, Clinical Sciences
Building, St. James's University Hospital, Leeds LS9 7TF,
United Kingdom. c.toomes@leeds.ac.uk
SOURCE: American Journal of Human Genetics, (2004) 74/4 (721-730).
Refs: 48
ISSN: 0002-9297 CODEN: AJHGAG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Familial exudative vitreoretinopathy (FEVR) is an inherited blinding
disorder of the retinal vascular system. Autosomal dominant FEVR is
genetically heterogeneous, but its principal locus, EVR1, is on chromosome
11q13-q23. The gene encoding the Wnt receptor frizzled-4 (FZD4) was
recently reported to be the EVR1 gene, but our mutation screen revealed
fewer patients harboring mutations than expected. Here, we describe
mutations in a second gene at the EVR1 locus, low-density-lipoprotein
receptor-related protein 5 (***LRP5***), a Wnt coreceptor. This
finding further underlines the significance of Wnt signaling in the
vascularization of the eye and highlights the potential dangers of using
multiple families to refine genetic intervals in gene-identification
studies.

L7 ANSWER 25 OF 68 MEDLINE on STN
DUPLICATE 10
ACCESSION NUMBER: 2004605612 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15578921
TITLE: Wnt/beta-catenin signaling pathway as a novel cancer drug
target.
AUTHOR: Luu Hue H; Zhang Ruiwen; Haydon Rex C; Rayburn Elizabeth;
Kang Quan; Si Weike; Park Jong Kyung; Wang Hui; Peng Ying;
Jiang Wei; He Tong-Chuan
CORPORATE SOURCE: Molecular Oncology Laboratory, Department of Surgery, The
University of Chicago Medical Center, Chicago, IL 60637,

USA.
SOURCE: Current cancer drug targets, (2004 Dec) 4 (8) 653-71. Ref: 291
Journal code: 101094211. ISSN: 1568-0096.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041207
Last Updated on STN: 20050211
Entered Medline: 20050210
AB ***Wnt*** ***proteins*** are a large family of secreted glycoproteins. ***Wnt*** ***proteins*** bind to the Frizzled receptors and ***LRP5*** /6 co-receptors, and through stabilizing the critical mediator beta-catenin, initiate a complex signaling cascade that plays an important role in regulating cell proliferation and differentiation. Deregulation of the canonical Wnt/beta-catenin signaling pathway, mostly by inactivating mutations of the APC tumor suppressor, or oncogenic mutations of beta-catenin, has been implicated in colorectal tumorigenesis. Although oncogenic mutations of beta-catenin have only been discovered in a small fraction of non-colon cancers, elevated levels of beta-catenin protein, a hallmark of activated canonical Wnt pathway, have been observed in most common forms of human malignancies, indicating that activation of this pathway may play an important role in tumor development. Over the past 15 years, our understanding of this signaling pathway has significantly improved with the identification of key regulatory proteins and the important downstream targets of beta-catenin/Tcf transactivation complex. Given the fact that Wnt/beta-catenin signaling is tightly regulated at multiple cellular levels, the pathway itself offers ample targeting nodal points for cancer drug development. In this review, we discuss some of the strategies that are being used or can be explored to target key components of the Wnt/beta-catenin signaling pathway in rational cancer drug discovery.

L7 ANSWER 26 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2005024652 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15651377
TITLE: Wnt coreceptor low density lipoprotein receptor related protein 5 (***LRP5***) mediates the bone formation and glucose induced insulin secretion.
AUTHOR: Sakai Juro
SOURCE: Nippon Ronen Igakkai zasshi. Japanese journal of geriatrics, (2004 Nov) 41 (6) 625-8.
Journal code: 7507332. ISSN: 0300-9173.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20050118
Last Updated on STN: 20050202
Entered Medline: 20050201

L7 ANSWER 27 OF 68 MEDLINE on STN
DUPLICATE 11
ACCESSION NUMBER: 2004148705 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15040835
TITLE: Cooperation between TGF-beta and Wnt pathways during chondrocyte and adipocyte differentiation of human marrow stromal cells.
AUTHOR: Zhou Shuanhu; Eid Karim; Glowacki Julie
CORPORATE SOURCE: Department of Orthopedic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.
SOURCE: Journal of bone and mineral research : official journal of the American Society for Bone and Mineral Research, (2004 Mar) 19 (3) 463-70.
Journal code: 8610640. ISSN: 0884-0431.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040326
Last Updated on STN: 20041219
Entered Medline: 20041119
AB Human marrow stromal cells have the potential to differentiate to chondrocytes or adipocytes. We show interactions between TGF-beta and Wnt signaling pathways during stimulation of chondrogenesis and inhibition of adipogenesis. Combining these signals may be useful in marrow stromal cell therapies. INTRODUCTION: Human bone marrow stromal cells (hMSCs) have the potential to differentiate to lineages of mesenchymal tissues, including cartilage, fat, bone, tendon, and muscle. Agents like transforming growth factor (TGF)-beta promote chondrocyte differentiation at the expense of adipocyte differentiation. In other processes, TGF-beta and Wnt/wingless signaling pathways play major roles in controling certain developmental events and activation of specific target genes. We tested whether these pathways interact during differentiation of chondrocytes and

adipocytes in human marrow stromal cells. MATERIALS AND METHODS: Both a line of human marrow stromal cells (KM101) and freshly isolated hMSCs were studied. Reverse transcriptase-polymerase chain reaction (RT-PCR), Western blot, and macroarrays were used for analysis of the modulation of TGF-beta1 on Wnt signaling-associated genes, chondrocyte differentiation genes, and TGFbeta/bone morphogenetic protein (BMP) signaling-associated genes in KM101 cells. Early passage hMSCs obtained from 42- and 58-year-old women were used for the effects of TGF-beta and/or Wnt (mimicked by LiCl) signals on chondrocyte and adipocyte differentiation in two-dimensional (2-D) cultures, 3-D pellet cultures, and collagen sponges. RESULTS: As indicated by macroarray, RT-PCR, and Western blot, TGF-beta activated genes in the TGF-beta/Smad pathway, upregulated Wnt2, Wnt4, Wnt5a, Wnt7a, Wnt10a, and Wnt co-receptor ***LRP5*** , and increased nuclear accumulation and stability of beta-catenin in KM101 cells. TGF-beta upregulated chondrocyte gene expression in KM101 cells and also stimulated chondrocyte differentiation and inhibited adipocyte differentiation in hMSCs, synergistically with Wnt signal. Finally, hMSCs cultured in 3-D collagen sponges were stimulated by TGF-beta1 to express aggrecan and collagen type II mRNA, whereas expression of lipoprotein lipase was inhibited. CONCLUSIONS: In summary, TGF-beta stimulated chondrocyte differentiation and inhibited adipocyte differentiation of hMSCs in vitro. The activation of both TGF-beta and Wnt signal pathways by TGF-beta, and synergy between TGF-beta and Wnt signals, supports the view that Wnt-mediated signaling is one of the mechanisms of TGF-beta's effects on chondrocyte and adipocyte differentiation of hMSCs.

L7 ANSWER 28 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004267144 EMBASE
TITLE: Genetic determinants of bone mass.
AUTHOR: Baldock P.A.; Eisman J.A.
CORPORATE SOURCE: J.A. Eisman, Bone and Mineral Research Program, Garvan Institute of Medical Research, University of New South Wales, 384 Victoria Street, Sydney, NSW 2010, Australia.
j.eisman@garvan.org.au
SOURCE: Current Opinion in Rheumatology, (2004) 16/4 (450-456).
Refs: 73
ISSN: 1040-8711 CODEN: CORHES
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose of review: This review examines recent advances in the analysis of genetic determinants of bone mass. It addresses both human and animal linkage studies as well as genetic manipulations in animals, inbred mouse models, and candidate gene analyses. Recent findings: Recent studies have implicated novel regulatory pathways in bone biology including both the neuroendocrine system and metabolic pathways linked to lipid metabolism. Variations in the lipoprotein receptor-related protein 5 (***LRP5***), part of the Wnt-frizzled pathway, were independently identified by linkage in high and low bone mass families. Subsequently, other high bone mass syndromes have been shown to have mutations in this gene. Neural studies have shown the skeletal regulatory activity of leptin and neuropeptide Y receptors via the hypothalamus. Subsequently, the .beta.-adrenergic pathway has been implicated, with important changes in bone mass. The lipoxygenase 12/15 pathway, identified through inbred mouse models and through pharmacologic studies with specific inhibitors, has also been shown to have important effects on bone mass. These studies exemplify the value of genetic models both to identify and then confirm pathways by mutational study and pharmacologic interventions. Continuing candidate gene studies often performed with multiple loci complement such discoveries. However, these studies have not focused on the clinical endpoint of fracture and few have included large enough groups to engender confidence in the associations reported, as such studies may require thousands of individuals. Interestingly, results often differ by ethnicity, age, or gender. A small proportion have examined whether relevant genes influence response to treatment. Summary: The combinations of human and animal genetic linkage studies have advanced understanding of the regulation of bone mass. Studies ranging from linkage to pharmacology provide optimism for new targets and treatments for osteoporosis.

L7 ANSWER 29 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2004283249 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15182694
TITLE: Wnt signaling: Ig-norrin the dogma.
AUTHOR: Clevers Hans

CORPORATE SOURCE: Hubrecht Laboratory, Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.. clevers@niob.knaw.nl
SOURCE: Current biology : CB, (2004 Jun 8) 14 (11) R436-7. Ref: 11
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040609
Last Updated on STN: 20040903
Entered Medline: 20040902
AB Secreted ***Wnt*** ***proteins*** trigger the intracellular Wnt signaling cascade upon engagement of dedicated Frizzled-Lrp receptor complexes. Unexpectedly, a non-Wnt ligand for this receptor complex has now been discovered. This novel ligand, Norrin, is mutated in the hereditary ocular Norrie syndrome.

L7 ANSWER 30 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004184668 EMBASE
TITLE: Glucocorticoid enhances the expression of dickkopf-1 in human osteoblasts: Novel mechanism of glucocorticoid-induced osteoporosis.
AUTHOR: Ohnaka K.; Taniguchi H.; Kawate H.; Nawata H.; Takayanagi R.
CORPORATE SOURCE: K. Ohnaka, Department of Geriatric Medicine, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.
oonaka@geriat.med.kyushu-u.ac.jp
SOURCE: Biochemical and Biophysical Research Communications, (21 May 2004) 318/1 (259-264).
Refs: 28
ISSN: 0006-291X CODEN: BBRCA
PUBLISHER IDENT.: S 0006-291X(04)00733-8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
033 Orthopedic Surgery
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To clarify the underlying mechanism of glucocorticoid-induced osteoporosis, we investigated the effect of glucocorticoid on the expression of dickkopf-1 (Dkk-1), an antagonist of Wnt signaling, in primary cultured human osteoblasts. Dexamethasone markedly induced the expression of mRNA for Dkk-1 in a dose- and time-dependent manner. The expression of Kremen1, a receptor for Dkk, did not change by the treatment with dexamethasone, while that of low-density lipoprotein receptor-related protein 5 (***LRP5***), a Wnt coreceptor, slightly decreased by the treatment with dexamethasone. Dexamethasone increased the transcriptional activity of the Dkk-1 gene promoter in human osteoblasts. Serial deletion and mutation analyses of the Dkk-1 promoter showed that one putative glucocorticoid responsive element-like sequence located from -788 to -774bp is essential for the enhancement of the Dkk-1 promoter activity by dexamethasone in human osteoblasts. Since the Wnt signal is now recognized as a crucial regulator for bone formation, the Dkk-1 enhanced by glucocorticoid may inhibit the Wnt signal in osteoblasts, which may be involved in the pathogenesis of glucocorticoid-induced osteoporosis.

L7 ANSWER 31 OF 68 MEDLINE on STN
DUPLICATE 12
ACCESSION NUMBER: 2004032104 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14731402
TITLE: A mechanism for Wnt coreceptor activation.
AUTHOR: Tamai Keiko; Zeng Xin; Liu Chunming; Zhang Xinjun; Harada Yuko; Chang Zhijie; He Xi
CORPORATE SOURCE: Division of Neuroscience, Children's Hospital, Department of Neurology, Harvard Medical School, Boston, MA 02115, USA.
SOURCE: Molecular cell, (2004 Jan 16) 13 (1) 149-56.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040121
Last Updated on STN: 20040310
Entered Medline: 20040309
AB ***LDL*** ***receptor*** ***related*** ***proteins*** ***5*** and 6 (***LRP5*** /6) and their Drosophila homolog Arrow are single-span transmembrane proteins essential for Wnt/beta-catenin signaling, likely via acting as Wnt coreceptors. How Wnt activates ***LRP5*** /6/Arrow to initiate signal transduction is not well defined. Here we show that a PPPSP motif, which is reiterated five times in the ***LRP5*** /6/Arrow intracellular domain, is necessary and sufficient to trigger Wnt/beta-catenin signaling. A single PPPSP motif, upon transfer

to the LDL receptor, fully activates the Wnt pathway, inducing complete
axis duplication in Xenopus and TCF/beta-catenin-responsive transcription
in human cells. We further show that Wnt signal-ing stimulates, and
requires, phosphorylation of the PPPSP motif, which creates an inducible
docking site for Axin, a scaffolding protein controlling beta-catenin
stability. Our study identifies a critical signaling module and a key
phosphorylation-dependent activation step of the Wnt receptor complex and
reveals a unifying logic for transmembrane signaling by Wnts, growth
factors, and cytokines.

L7 ANSWER 32 OF 68 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2004639120 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15615112
TITLE: The high bone mass family--the role of Wnt/ ***Lrp5***
signaling in the regulation of bone mass.
AUTHOR: Johnson M L
CORPORATE SOURCE: Osteoporosis Research Center, Creighton University School
of Medicine, Omaha, NE 68131, USA.. MARKL@creighton.edu
SOURCE: J Musculoskelet Neuronal Interact, (2004 Jun) 4 (2) 135-8.
Ref: 23
Journal code: 101084496. ISSN: 1108-7161.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20041224
Last Updated on STN: 20050125
Entered Medline: 20050124
AB A G171V mutation in the low-density lipoprotein receptor-related protein 5
(***LRP5***) was identified as causal for an autosomal dominant high
bone mass trait in a single human family. A transgenic mouse line was
produced that carries this mutation and develops a high bone mass
phenotype that recapitulates the human phenotype. ***LRP5*** is a
co-receptor for Wnt and we have investigated the potential role of this
gene/protein and the Wnt signaling pathway in mediating the bone formation
response to mechanical loading. The G171V mutation results in an
increased responsiveness of bone to mechanical load and reduces the
threshold of load required to elicit a response. Our studies have shown
that the Wnt signaling pathway is activated in response to mechanical
loading and this response is greatly enhanced in the presence of the G171V
mutation. Additionally, this mutation results in increased transcription
of osteoprotegerin (OPG) in response to loading. Thus, the mutation
appears to have direct effects at the level of the osteoblast and may also
result in a reduction in osteoclastogenesis. The identification of
LRP5 /Wnt signaling in bone mechanosensation has resulted in a new
paradigm for understanding bone formation. Hopefully, knowledge gained
from these studies will result in new therapies for treating osteoporosis.

L7 ANSWER 33 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004057679 EMBASE
TITLE: Expression of ***LDL*** ***receptor*** -
related ***protein*** ***5*** (***LRP5***
) as a novel marker for disease progression in high-grade
osteosarcoma.
AUTHOR: Hoang B.H.; Kubo T.; Healey J.H.; Sowers R.; Mazza B.; Yang
R.; Huvos A.G.; Meyers P.A.; Gorlick R.
CORPORATE SOURCE: R. Gorlick, Department of Pediatrics, Mem. Sloan-Kettering
Cancer Center, Box 376, 1275 York Avenue, New York, NY
10021, United States
SOURCE: International Journal of Cancer, (10 Mar 2004) 109/1
(106-111).
Refs: 32
ISSN: 0020-7136 CODEN: IJCNAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The Wingless-type (Wnt) family of proteins and its coreceptor ***LRP5***
have recently been implicated in human skeletal development. Wnt pathway
modulates cell fate and cell proliferation during embryonic development
and carcinogenesis through activation of receptor-mediated signaling.
Osteosarcoma (OS) is a bone-forming tumor of mesenchymal origin whose
growth control has been linked to autocrine or paracrine stimulation by
several growth factor families. We examined 4 OS cell lines for WNT1,
WNT4, WNT5A, WNT7A, WNT11, FZDI-10 and ***LRP5*** expression by
reverse transcription polymerase chain reaction (RT-PCR). In addition,
RT-PCR for ***LRP5*** expression was performed in 44 OS patient
samples and the findings were correlated with clinical data. Expression

profiling of Wnts and their receptors revealed the presence of several isoforms in OS cell lines. Overall, 22/44 (50%) of OS patient samples showed evidence of ***LRP5*** expression. Presence of ***LRP5*** correlated significantly with tumor metastasis (p = 0.005) and the chondroblastic subtype of OS (p = 0.045). In addition, patients whose tumors were positive for ***LRP5*** showed a trend toward decreased event-free survival (p = 0.066). No significant association was found between ***LRP5*** expression and age, gender, site of disease, site of metastasis or degree of chemotherapy-induced tumor necrosis. Sequencing of exon 3 of ***LRP5*** in 10 OS patient-derived cell cultures showed no activating mutation of ***LRP5*** . These results showed that expression of ***LRP5*** is a common event in OS and strongly suggest a role for LRP and Wnt signaling in the pathobiology and progression of this disease. .COPYRGT. 2003 Wiley-Liss, Inc.

L7 ANSWER 34 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2004199481 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15095618
TITLE: [Wnt/ ***LRP5*** , a new regulation osteoblastic pathway involved in reaching peak bone masses]. Wnt/ ***LRP5*** , une nouvelle voie de regulation osteoblastique impliquee dans l'acquisition du pic de masses osseuses.
AUTHOR: Caverzasio Joseph
CORPORATE SOURCE: Service des maladies osseuses Departement de rehabilitation et geriatrie HUG.. Joseph.Caverzasio@medecine.unige.ch
SOURCE: Revue medicale de la Suisse romande, (2004 Feb) 124 (2) 81-2. Journal code: 0421524. ISSN: 0035-3655.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040421 Last Updated on STN: 20040521 Entered Medline: 20040520
AB With the ageing of the population in industrial countries, osteoporosis became an important concern of public health. For an efficacious treatment of this disease, we would need drugs capable of selectively and safely increasing bone volume. Recent genetic analyses revealed a new signaling pathway involved in the regulation of osteoblastic cells and the acquisition of pic bone mass. Loss or gain of function mutations in the ***LRP5*** gene have been found to be associated with correspondingly low or high bone mass syndromes. Loss of function is associated with juvenile osteoporosis, whereas gain of function leads to the high bone mass syndrome. Recent studies have shown that ***LRP5*** is implicated in the regulation of the proliferation and of the activity of osteoblastic cells. By analogy with other cellular systems, it has been suggested that ***LRP5*** plays a role in the Wnt signaling system. ***Wnt*** ***proteins*** are known to be involved in developmental processes and the implication of this system in controlling osteoblastic activity and bone formation was completely unexpected. Analysis of the cellular mechanism by which Wnt/ ***LRP5*** activates osteoblastic cells is of potential interest for the development of new molecules capable of selectively increasing bone mass for the treatment of osteoporosis.

L7 ANSWER 35 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2004603043 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15576958
TITLE: Recent topics on bone remodeling.
AUTHOR: Shinoda Yusuke; Ogata Naoshi; Chung Ung Il; Kawaguchi Hiroshi
CORPORATE SOURCE: Department of Orthopaedic Surgery and Division of Tissue Engineering, University of Tokyo Hospital, Tokyo, Japan.
SOURCE: Clin Calcium, (2004 Jan) 14 (1) 70-4. Ref: 28 Journal code: 9433326. ISSN: 0917-5857.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041204 Last Updated on STN: 20041230 Entered Medline: 20041229
AB The Wnt signaling pathway has recently been demonstrated to play an important role in regulation of bone formation. ***LRP5*** is thought to signal through the canonical Wnt pathway. In humans, ***LRP5*** loss-of-function mutations lead to low bone mass with fractures, while ***LRP5*** gain-of-function mutations lead to high bone mass, thus identifying ***LRP5*** as an important regulator of bone mass. Patients with sclerosteosis have a severe skeletal disorder with progressive bone overgrowth due to a loss of function of the SOST gene, which implicates its role as a suppressor of bone formation. Recent study

revealed that SOST is a BMP antagonist with unique ligand specificity,
negatively regulating bone formation by repressing BMP-induced osteoblast
differentiation or function or both.

L7 ANSWER 36 OF 68 MEDLINE on STN
DUPLICATE 14
ACCESSION NUMBER: 2004030873 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14729180
TITLE: The ins and outs of Wingless signaling.
AUTHOR: Seto Elaine S; Bellen Hugo J
CORPORATE SOURCE: Program in Developmental Biology, Department of Molecular
and Human Genetics, Division of Neuroscience, Baylor
College of Medicine, Houston, TX 77030, USA.
SOURCE: Trends in cell biology, (2004 Jan) 14 (1) 45-53. Ref: 71
Journal code: 9200566. ISSN: 0962-8924.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040121
Last Updated on STN: 20040820
Entered Medline: 20040819
AB Signaling through the highly conserved Wingless/Wnt pathway plays a
crucial role in a diverse array of developmental processes, many of which
depend upon the precise regulation of Wingless/Wnt signaling levels.
Recent evidence has indicated that the intracellular trafficking of
Wingless/Wnt signaling components can result in significant changes in the
level of signaling. Here, we examine three mechanisms through which
intracellular trafficking might regulate Wingless signaling--the
degradation of Wingless, its transport and the transduction of its signal.
The intracellular trafficking of several Wingless/Wnt signaling
components, including ***LRP5*** , LRP6, Dishevelled and Axin, as well
as the functional implications of protein localization on Wingless/Wnt
signaling, will be discussed.

L7 ANSWER 37 OF 68 MEDLINE on STN
DUPLICATE 15
ACCESSION NUMBER: 2004505926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15474285
TITLE: Wnt signaling in osteoblasts and bone diseases.
AUTHOR: Westendorf Jennifer J; Kahler Rachel A; Schroeder Tania M
CORPORATE SOURCE: The Cancer Center and Department of Orthopaedic Surgery,
University of Minnesota, MMC 806, 420 Delaware St. SE,
Minneapolis, MN 55455, USA..
weste047@umn.edu
SOURCE: Gene, (2004 Oct 27) 341 19-39. Ref: 219
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20041013
Last Updated on STN: 20050114
Entered Medline: 20050113
AB Recent revelations that the canonical Wnt signaling pathway promotes
postnatal bone accrual are major advances in our understanding of skeletal
biology and bring tremendous promise for new therapeutic treatments for
osteoporosis and other diseases of altered bone mass. Wnts are soluble
glycoproteins that engage receptor complexes composed of ***Lrp5*** /6
and Frizzled proteins. A subgroup of Wnts induces a cascade of
intracellular events that stabilize beta-catenin, facilitating its
transport to nuclei where it binds Lef1/Tcf transcription factors and
alters gene expression to promote osteoblast expansion and function.
Natural extracellular Wnt antagonists, Dickkopfs and secreted
frizzled-related proteins, impair osteoblast function and block bone
formation. In several genetic disorders of altered skeletal mass,
mutations in ***LRP5*** create gain-of-function or loss-of-function
receptors that are resistant to normal regulatory mechanisms and cause
higher or lower bone density, respectively. In this review, we summarize
the available molecular, cellular, and genetic data that demonstrate how
Lrp5 and other components of the Wnt signaling pathway influence
osteoblast proliferation, function, and survival. We also discuss
regulatory mechanisms discovered in developmental and tumor models that
may provide insights into novel therapies for bone diseases.

L7 ANSWER 38 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:737597 CAPLUS
DOCUMENT NUMBER: 139:240388
TITLE: Novel application and function of Wnt in the treatment
of diabetes and hyperlipemia
INVENTOR(S): Yamamoto, Tokuo; Sakai, Juro; Fujino, Takahiro
PATENT ASSIGNEE(S): Anges MG, Inc., Japan
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075948	A1	20030918	WO 2003-JP2719	20030307

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-64458 A 20020308

AB Drugs contg. ***Wnt*** ***protein*** or a gene encoding ***Wnt*** ***protein*** and having an effect of promoting insulin secretion or ameliorating lipid metab.; a method of identifying an agonist to ***LRP5*** /6; and a method of identifying a compd. controlling the expression of ***Wnt*** ***protein*** and ***LRP5*** /6 in cells. The agonist and the compd. identified these methods are useful in treating or preventing, in particular, diabetes, hyperlipemia or impaired glucose tolerance, similar to drugs contg. Wnt.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 39 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2003:330153 USPATFULL
TITLE: Diagnosis, prognosis and identification of potential therapeutic targets of multiple myeloma based on gene expression profiling
INVENTOR(S): Shaughnessy, John D., Little Rock, AR, UNITED STATES
Barlogie, Bart, Little Rock, AR, UNITED STATES
Zhan, Fenghuang, Little Rock, AR, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003232364	A1	20031218
APPLICATION INFO.:	US 2003-409004	A1	20030408 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-289746, filed on 7 Nov 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-403075P	20020813 (60)
	US 2001-348238P	20011107 (60)
	US 2002-355386P	20020208 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Dr. Benjamin Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 4100
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Gene expression profiling between normal B cells/plasma cells and multiple myeloma cells revealed four distinct subgroups of multiple myeloma plasma cells that have significant correlation with clinical characteristics known to be associated with poor prognosis. Diagnosis for multiple myeloma (and possibly monoclonal gammopathy of undetermined significance) based on differential expression of 14 genes, as well as prognostics for the four subgroups of multiple myeloma based on the expression of 24 genes were also established. Gene expression profiling also allows placing multiple myeloma into a developmental schema parallel to that of normal plasma cell differentiation. The development of a gene expression- or developmental stage-based classification system for multiple myeloma would lead to rational design of more accurate and sensitive diagnostics, prognostics and tumor-specific therapies for multiple myeloma.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 40 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2003:237344 USPATFULL
TITLE: Treatment involving Dkk-1 or antagonists thereof
INVENTOR(S): DeAlmeida, Venita I., San Carlos, CA, UNITED STATES
Stewart, Timothy A., San Francisco, CA, UNITED STATES
PATENT ASSIGNEE(S): GENENTECH, INC. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003165501	A1	20030904
APPLICATION INFO.:	US 2002-77065	A1	20020215 (10)

	NUMBER	DATE

PRIORITY INFORMATION: US 2001-269435P 20010216 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA, 94080
NUMBER OF CLAIMS: 52
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 3365
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antagonists to Dickkopf-1 (Dkk-1) protein are administered in effective amounts to treat disorders involving insulin resistance, such as non-insulin-dependent diabetes mellitus (NIDDM), hypoinsulinemia, and disorders involving muscle atrophy, trauma, or degeneration. Preferably, the antagonists are composed of compositions comprising antibodies directed to Dkk-1 in a pharmaceutically acceptable carrier for use in blocking the effects of Dkk-1. Additionally provided is a method of treating obesity or hyperinsulinemia in a mammal by administering an effective amount of Dkk-1 to a mammal. Also provided are methods of diagnosing insulin resistance, hyper- and hypoinsulinemia, obesity, and related disorders using Dkk-1 as a target and non-human transgenic animals that overexpress dkk-1 nucleic acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 41 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2003:237343 USPATFULL
TITLE: Wnt and frizzled receptors as targets for immunotherapy in head and neck squamous cell carcinomas
INVENTOR(S): Rhee, Chae-Seo, Seoul, KOREA, REPUBLIC OF
Sen, Malini, San Diego, CA, UNITED STATES
Wu, Christina, San Diego, CA, UNITED STATES
Leoni, Lorenzo M., San Diego, CA, UNITED STATES
Corr, Maripat, San Diego, CA, UNITED STATES
Carson, Dennis A., Del Mar, CA, UNITED STATES
PATENT ASSIGNEE(S): REGENTS OF THE UNIVERSITY OF CALIFORNIA, Oakland, CA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003165500	A1	20030904
APPLICATION INFO.:	US 2002-285976	A1	20021101 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2002-US13802, filed on 1 May 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-287995P	20010501 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 140
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Page(s)
LINE COUNT: 7969
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The diverse receptor-ligand pairs of the Wnt and frizzled (Fzd) families play important roles during embryonic development, and thus may be overexpressed in cancers that arise from immature cells. The mRNA levels and expression levels of 5 Wnt (Wnt-1, 5a, 7a, 10b, 13) and 2 Fzd (Fzd-2, 5) genes in 10 head and neck squamous carcinoma cell lines (HNSCC) were investigated. In addition, anti-Wnt-1 antibodies were used to study the Wnt/Fzd signalling pathway. These results indicate that HNSCC cell lines overexpress one or more Wnt and Fzd genes, and the proliferation and survival of a subset of HNSCC may depend on the Wnt/Fzd pathway. Therefore, the Wnt and Fzd receptors may be useful targets for immunotherapy of this common cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 42 OF 68 USPATFULL on STN
ACCESSION NUMBER: 2003:37506 USPATFULL
TITLE: Regulator gene and system useful for the diagnosis and therapy of osteoporosis
INVENTOR(S): Warman, Matthew L., Shaker Heights, OH, UNITED STATES
Gong, Yaoqin, Jinan, CHINA
Olsen, Bjorn R., Milton, MA, UNITED STATES
Rawadi, Georges, Paris, FRANCE
Roman-Roman, Sergio, Paris, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003027151	A1	20030206
APPLICATION INFO.:	US 2001-931375	A1	20010817 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-304851P	20010713 (60)
	US 2000-226119P	20000818 (60)
	US 2000-234337P	20000922 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 3896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A bone strength and mineralization regulatory ("BSMR") protein is provided that can exist in multiple forms and that affects bone density. Polymorphic gene sequences of the protein are provided that are diagnostic of predipostion to osteoporosis. Other detection tools, compositions and methods of their use also are provided for predicting, evaluating and altering bone strength and mineralization status. The invention provides new natural and synthetic pharmaceuticals that effect the BSMR regulatory pathway and improve bone status. Tools also are provided for finding new pharmaceuticals that operate by binding to BSMR and that activate and/or deactivate this protein's biological function related to osteoporosis and blood vessel formation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 43 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2003149709 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12551949
TITLE: Lymphoid enhancer factor-1 and beta-catenin inhibit Runx2-dependent transcriptional activation of the osteocalcin promoter.
AUTHOR: Kahler Rachel A; Westendorf Jennifer J
CORPORATE SOURCE: University of Minnesota Cancer Center, Department of Orthopaedic Surgery and Graduate Program in Microbiology, Immunology and Cancer Biology, Minneapolis, Minnesota 55455, USA.
SOURCE: Journal of biological chemistry, (2003 Apr 4) 278 (14) 11937-44.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030401
Last Updated on STN: 20030520
Entered Medline: 20030519
AB Functional control of the transcription factor Runx2 is crucial for normal bone formation. Runx2 is detectable throughout osteoblast development and maturation and temporally regulates several bone-specific genes. In this study, we identified a novel post-translational mechanism regulating Runx2-dependent activation of the osteocalcin promoter. A functional binding site for the high mobility group protein lymphoid enhancer-binding factor 1 (LEF1) was found adjacent to the proximal Runx2-binding site in the osteocalcin promoter. In transcription assays, LEF1 repressed Runx2-induced activation of the mouse osteocalcin 2 promoter in several osteoblast lineage cell lines. Mutations in the LEF1-binding site increased the basal activity of the osteocalcin promoter; however, the LEF1 recognition site in the osteocalcin promoter was surprisingly not required for LEF1 repression. A novel interaction between the DNA-binding domains of Runx2 and LEF1 was identified and found crucial for LEF1-mediated repression of Runx2. LEF1 is a nuclear effector of the Wnt/ ***LRP5*** /beta-catenin signaling pathway, which is also essential for osteoblast proliferation and normal skeletal development. A constitutively active beta-catenin enhanced LEF1-dependent repression of Runx2. These data identify a novel mechanism of regulating Runx2 activity in osteoblasts and link Runx2 transcriptional activity to beta-catenin signaling.

L7 ANSWER 44 OF 68 MEDLINE on STN
DUPLICATE 16
ACCESSION NUMBER: 2003508144 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14584895
TITLE: BMP-2 controls alkaline phosphatase expression and osteoblast mineralization by a Wnt autocrine loop.
AUTHOR: Rawadi Georges; Vayssiere Beatrice; Dunn Fred; Baron Roland; Roman-Roman Sergio
CORPORATE SOURCE: Proskelia Pharmaceuticals, Romainville, France.. georges.rawadi@proskelia.com
SOURCE: Journal of bone and mineral research : official journal of the American Society for Bone and Mineral Research, (2003 Oct) 18 (10) 1842-53.
Journal code: 8610640. ISSN: 0884-0431.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20031031
Last Updated on STN: 20040603
Entered Medline: 20040602
AB Wnt/beta-catenin signaling has recently been suggested to be involved in bone biology. The precise role of this cascade in osteoblast

differentiation was examined. We show that a Wnt autocrine loop mediates
the induction of alkaline phosphatase and mineralization by BMP-2 in
pre-osteoblastic cells. INTRODUCTION: Loss of function of ***LRP5***
leads to osteoporosis (OPPG syndrome), and a specific point mutation in
this same receptor results in high bone mass (HBM). Because ***LRP5***
acts as a coreceptor for ***Wnt*** ***proteins*** , these findings
suggest a crucial role for Wnt signaling in bone biology. MATERIALS AND
METHODS: We have investigated the involvement of the Wnt/ ***LRP5***
cascade in osteoblast function by using the pluripotent mesenchymal cell
lines C3H10T1/2, C2C12, and ST2 and the osteoblast cell line MC3T3-E1.
Transfection experiments were carried out with a number of elements of the
Wnt/ ***LRP5*** pathway. Measuring osteoblast and adipocyte
differentiation markers addressed the effect of this cascade on osteoblast
differentiation. RESULTS: In mesenchymal cells, only Wnt's capable of
stabilizing beta-catenin induced the expression of alkaline phosphatase
(ALP). Wnt3a-mediated ALP induction was inhibited by overexpression of
either Xddl, dickkopf 1 (dkk1), or LRP5deltaC, indicating that canonical
beta-catenin signaling is responsible for this activity. The use of
Noggin, a bone morphogenic protein (BMP) inhibitor, or cyclopamine, a
Hedgehog inhibitor, revealed that the induction of ALP by Wnt is
independent of these morphogenetic proteins and does not require de novo
protein synthesis. In contrast, blocking Wnt/ ***LRP5*** signaling or
protein synthesis inhibited the ability of both BMP-2 and Shh to induce
ALP in mesenchymal cells. Moreover, BMP-2 enhanced Wntl and Wnt3a
expression in our cells. In MC3T3-E1 cells, where endogenous ALP levels
are maximal, antagonizing the Wnt/ ***LRP5*** pathway led to a decrease
of ALP activity. In addition, overexpression of dkkl reduced
extracellular matrix mineralization in a BMP-2-dependent assay.
CONCLUSIONS: Our data strongly suggest that the capacity of BMP-2 and Shh
to induce ALP relies on Wnt expression and the Wnt/ ***LRP5***
signaling cascade. Moreover the effects of BMP-2 on extracellular matrix
mineralization by osteoblasts are mediated, at least in part, by the
induction of a Wnt autocrine/paracrine loop. These results may help to
explain the phenotype of OPPG patients and HBM.

on STN DUPLICATE 17
ACCESSION NUMBER: 2003141629 EMBASE
TITLE: Wnt signaling in B-cell neoplasia.
AUTHOR: Qiang Y.-W.; Endo Y.; Rubin J.S.; Rudikoff S.
CORPORATE SOURCE: S. Rudikoff, Lab. of Cell. and Molecular Biology, National
Cancer Institute, NIH, Bethesda, MD 20892, United States.
Rudikoff@helix.nih.gov
SOURCE: Oncogene, (13 Mar 2003) 22/10 (1536-1545).
Refs: 39
ISSN: 0950-9232 CODEN: ONCNES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Wnts comprise a family of secreted proteins that interact with receptors
consisting of a Frizzled (Fz) family member alone or complexed with LDL
receptor-related proteins (***LRP5*** /6). Wnt signaling plays a
crucial role in both development and differentiation, and activation of a
'canonical' Wnt pathway resulting in .beta.-catenin stabilization is
associated with several types of human cancers. To date, little is known
about potential Wnt signaling in mature lymphocytes or lymphoid neoplasia.
Herein, we have analysed Wnt signaling in mature B cells (lymphomas) and
plasma cells (multiple myeloma). Both Fz and ***LRP5*** /6 mRNAs were
expressed in myeloma lines, but ***LRP5*** /6 were not observed in
lymphomas. In myelomas, a canonical Wnt signaling pathway was activated
following treatment with Wnt-3a as assessed by accumulation of
.beta.-catenin, but .beta.-catenin levels actually decreased in lymphoma
cells. Wnt-3a treatment further led to striking morphological changes in
myeloma cells accompanied by rearrangement of the actin cytoskeleton.
Morphological changes were associated with a second Wnt pathway dependent
on Rho activation. These results suggest that Wnt responsiveness is a
stage-specific phenomenon in B-cell development and that the morphological
changes associated with Wnt signaling may play a role in the motility and
metastatic potential of myeloma cells.

on STN DUPLICATE 18
ACCESSION NUMBER: 2003424757 EMBASE
TITLE: High Bone Mass in Mice Expressing a Mutant ***LRP5***
Gene.
AUTHOR: Babij P.; Zhao W.; Small C.; Kharode Y.; Yaworsky P.J.;
Bouxsein M.L.; Reddy P.S.; Bodine P.V.; Robinson J.A.; Bhat

B.; Marzolf J.; Moran R.A.; Bex F.
CORPORATE SOURCE: Dr. F. Bex, Women's Health Research Institute, Wyeth
Research, 500 Arcola Road, Collegeville, PA 19426, United
States. bexf@wyeth.com
SOURCE: Journal of Bone and Mineral Research, (1 Jun 2003) 18/6
(960-974).
Refs: 46
ISSN: 0884-0431 CODEN: JBMREJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A unique mutation in ***LRP5*** is associated with high bone mass in
man. Transgenic mice expressing this ***LRP5*** mutation have a
similar phenotype with high bone mass and enhanced strength. These results
underscore the importance of ***LRP5*** in skeletal regulation and
suggest targets for therapies for bone disease. A mutation (G171V) in the
low-density lipoprotein receptor related protein 5 (***LRP5***) has
been associated with high bone mass (HBM) in two independent human
kindreds. To validate the role of the mutation, several lines of
transgenic mice were created expressing either the human ***LRP5***
G171V substitution or the wildtype ***LRP5*** gene in bone. Volumetric
bone mineral density (vBMD) analysis by pQCT showed dramatic increases in
both total vBMD (30-55%) and trabecular vBMD (103-250%) of the distal
femoral metaphysis and increased cortical size of the femoral diaphysis in
mutant G171V transgenics at 5, 9, 17, 26, and 52 weeks of age ($p < 0.01$
for all). In addition, high-resolution microcomputed tomography (microCT)
analysis of the distal femorae and lumbar vertebrae revealed an increase
(110-232%) in trabecular bone volume fraction caused by both increased
trabecular number (41-74%) and increased trabecular thickness (34-46%; $p <$
0.01 for all) in the mutant G171V mice. The increased bone mass was
associated with significant increases in vertebral compressive strength
(80-140%) and the increased cortical size with significant increases in
femoral bending strength (50-130%). There were no differences in
osteoclast number at 17 weeks of age. However, compared with littermate
controls, the mutant G171V transgenic mice showed an increase in actively
mineralizing bone surface, enhanced alkaline phosphatase staining in
osteoblasts, and a significant reduction in the number of TUNEL-positive
osteoblasts and osteocytes. These results suggest that the increased bone
mineral density in mutant G171V mice was caused by increased numbers of
active osteoblasts, which could in part be because of their increased
functional lifespan. While slight bone anabolic activity was observed from
overexpression of the wildtype ***LRP5*** gene, it is clear that the
G171V mutation, rather than overexpression of the receptor itself, is
primarily responsible for the dramatic HBM bone effects. Together, these
findings establish the importance of this novel and unexpected role of a
lipoprotein receptor in regulating bone mass and afford a new model to
explore ***LRP5*** and its recent association with Wnt signaling in
bone biology.

L7 ANSWER 47 OF 68 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN DUPLICATE 19
ACCESSION NUMBER: 2003:202905 BIOSIS
DOCUMENT NUMBER: PREV200300202905
TITLE: Wg/Wnt signal can be transmitted through Arrow/ ***LRP5***
,6 and Axin independently of Zw3/Gsk3beta activity.
AUTHOR(S): Tolwinski, Nicholas S.; Wehrli, Marcel; Rives, Anna;
Erdeniz, Naz; DiNardo, Stephen; Wieschaus, Eric [Reprint
Author]
CORPORATE SOURCE: Howard Hughes Medical Institute, Princeton University,
Princeton, NJ, 08544, USA
ewieschaus@molbio.princeton.edu
SOURCE: Developmental Cell, (March 2003) Vol. 4, No. 3, pp.
407-418. print.
ISSN: 1534-5807 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Apr 2003
Last Updated on STN: 23 Apr 2003
AB Activation of the Wnt signaling cascade provides key signals during
development and in disease. Here we provide evidence, by designing a Wnt
receptor with ligand-independent signaling activity, that physical
proximity of Arrow (LRP) to the Wnt receptor Frizzled-2 triggers the
intracellular signaling cascade. We have uncovered a branch of the Wnt
pathway in which Armadillo activity is regulated concomitantly with the
levels of Axin protein. The intracellular pathway bypasses Gsk3beta/Zw3,
the kinase normally required for controlling beta-catenin/Armadillo
levels, suggesting that modulated degradation of Armadillo is not required
for Wnt signaling. We propose that Arrow (LRP) recruits Axin to the
membrane, and that this interaction leads to Axin degradation. As a

consequence, Armadillo is no longer bound by Axin, resulting in nuclear
signaling by Armadillo.

L7 ANSWER 48 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 20
ACCESSION NUMBER: 2003070945 EMBASE
TITLE: MESD encodes an ***LRP5*** /6 chaperone essential for
specification of mouse embryonic polarity.
AUTHOR: Hsieh J.-C.; Lee L.; Zhang L.; Wefer S.; Brown K.; DeRossi
C.; Wines M.E.; Rosenquist T.; Holdener B.C.
CORPORATE SOURCE: B.C. Holdener, Dept. of Biochem. and Cell Biology, Center
for Developmental Genetics, State University of New York,
Stony Brook, NY 11794, United States.
bernadette.holdener@stonybrook.edu
SOURCE: Cell, (7 Feb 2003) 112/3 (355-367).
Refs: 39
ISSN: 0092-8674 CODEN: CELLB5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Specification of embryonic polarity and pattern formation in multicellular
organisms requires inductive signals from neighboring cells. One approach
toward understanding these interactions is to study mutations that disrupt
development. Here, we demonstrate that mesd, a gene identified in the
mesoderm development (mesd) deletion interval on mouse chromosome 7, is
essential for specification of embryonic polarity and mesoderm induction.
MESD functions in the endoplasmic reticulum as a specific chaperone for
LRP5 and LRP6, which in conjunction with Frizzled, are coreceptors
for canonical WNT signal transduction. Disruption of embryonic polarity
and mesoderm differentiation in mesd-deficient embryos likely results from
a primary defect in WNT signaling. However, phenotypic differences between
mesd-deficient and wnt3(-/-) embryos suggest that MESD may function on
related members of the low-density lipoprotein receptor (LDLR) family,
whose members mediate diverse cellular processes ranging from cargo
transport to signaling.

L7 ANSWER 49 OF 68 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 2003:278772 BIOSIS
DOCUMENT NUMBER: PREV200300278772
TITLE: The ***LRP5*** gene is involved in different conditions
with an increased bone density as illustrated by the
identification of six novel missense mutations.
AUTHOR(S): Van Wesenbeeck, L. [Reprint Author]; Cleiren, E. [Reprint
Author]; Gram, J.; Beals, R. K.; Warman, M. L.;
deVernejoul, M. C.; Bollerslev, J.; Van Hul, W. [Reprint
Author]
CORPORATE SOURCE: Dept. Medical Genetics, University of Antwerp, Antwerp,
Belgium
SOURCE: Calcified Tissue International, (April 2003) Vol. 72, No.
4, pp. 327. print.
Meeting Info.: 30th European Symposium on Calcified
Tissues. Rome, Italy. May 08-12, 2003.
CODEN: CTINDZ. ISSN: 0171-967X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

L7 ANSWER 50 OF 68 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on
STN
ACCESSION NUMBER: 2003:278720 BIOSIS
DOCUMENT NUMBER: PREV200300278720
TITLE: Role of the WNT/ ***LRP5*** pathway in regulation of
bone mass and osteoblast function.
AUTHOR(S): Warman, M. [Reprint Author]
CORPORATE SOURCE: Cleveland, OH, USA
SOURCE: Calcified Tissue International, (April 2003) Vol. 72, No.
4, pp. 314. print.
Meeting Info.: 30th European Symposium on Calcified
Tissues. Rome, Italy. May 08-12, 2003.
CODEN: CTINDZ. ISSN: 0171-967X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

L7 ANSWER 51 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 21
ACCESSION NUMBER: 2003162201 EMBASE
TITLE: Axin and the Axin/Arrow-binding protein DCAP mediate
glucose-glycogen metabolism.
AUTHOR: Yamazaki H.; Yanagawa S.-I.
CORPORATE SOURCE: H. Yamazaki, Department of Cell Biology, Harvard Medical
School, 240 Longwood Avenue, Boston, MA 02115, United
States. hyamazaki@hms.harvard.edu
SOURCE: Biochemical and Biophysical Research Communications, (2 May
2003) 304/2 (229-235).
Refs: 33
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
029 Clinical Biochemistry
LANGUAGE: English

SUMMARY LANGUAGE: English
AB Axin was found as a negative regulator of the canonical Wnt pathway. Human
LRP5 was originally found as a candidate gene of insulin dependent
diabetes mellitus (IDDM), but its Drosophila homolog, Arrow, works as a
co-receptor of the canonical Wnt signal. In our previous paper, we found a
new Drosophila Axin (Daxin)-binding SH3 protein, DCAP, a homolog of
mammalian CAV family protein. Among the subtypes, DCAPL3 shows significant
homology with CAP, an essential component of glucose transport in insulin
signal. Further binding assay revealed that DCAP binds to not only Axin
but also Arrow, and Axin binds to not only GSK3.beta. but also Arrow.
However, overexpression and RNAi experiments of DCAP do not affect the
canonical Wnt pathway. As DCAP is expressed predominantly in
insulin-target organs, and as RNAi of DCAP disrupts the pattern of
endogenous glycogen accumulation in late stage embryos, we suggest that
DCAP is also involved in glucose transport. Moreover, early stage embryos
lacking maternal Axin show significant delay of initial glycogen
decomposition, and RNAi of Axin in S2 cells revealed quite increase of
endogenous glycogen level as well as GSK3.beta.. These results suggest
that Axin and DCAP mediate glucose-glycogen metabolism in embryo. In
addition, the interaction among Axin, Arrow, and DCAP implies a possible
cross-talk between Wnt signal and insulin signal.

L7 ANSWER 52 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2003030437 EMBASE
TITLE: Low-density lipoprotein receptor-related protein 5 (***LRP5***) is essential for normal cholesterol
metabolism and glucose-induced insulin secretion.
AUTHOR: Fujino T.; Asaba H.; Kang M.-J.; Ikeda Y.; Sone H.; Takada
S.; Kim D.-H.; Ioka R.X.; Ono M.; Tomoyori H.; Okubo M.;
Murase T.; Kamataki A.; Yamamoto J.; Magoori K.; Takahashi
S.; Miyamoto Y.; Oishi H.; Nose M.; Okazaki M.; Usui S.;
Imaizumi K.; Yanagisawa M.; Sakai J.; Yamamoto T.T.
CORPORATE SOURCE: J. Sakai, Yanagisawa Orphan Receptor Project, Exploratory
Res. for Adv. Technology, Japan Sci. and Technol.
Corporation, 2-41, Aomi, Koto-ku, Tokyo 135-0064, Japan.
jmsakai@maii.cc.tohoku.ac.jp
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (7 Jan 2003) 100/1 (229-234).
Refs: 39
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A Wnt coreceptor low-density lipoprotein receptor-related protein 5 (
LRP5) plays an essential role in bone accrual and eye development.
Here, we show that ***LRP5*** is also required for normal cholesterol
and glucose metabolism. The production of mice lacking ***LRP5***
revealed that ***LRP5*** deficiency led to increased plasma
cholesterol levels in mice fed a high-fat diet, because of the decreased
hepatic clearance of chylomicron remnants. In addition, when fed a normal
diet, ***LRP5*** -deficient mice showed a markedly impaired glucose
tolerance. The LRPS-deficient islets had a marked reduction in the levels
of intracellular ATP and Ca(2+) in response to glucose, and thereby
glucose-induced insulin secretion was decreased. The intracellular
inositol 1,4,5-trisphosphate (IP3) production in response to glucose was
also reduced in ***LRP5*** -/- islets. Real-time PCR analysis revealed
a marked reduction of various transcripts for genes involved in glucose
sensing in ***LRP5*** -/- islets. Furthermore, exposure of ***LRP5***
+/+ islets to Wnt-3a and Wnt-5a stimulates glucose-induced insulin
secretion and this stimulation was blocked by the addition of a soluble
form of Wnt receptor, secreted Frizzled-related protein-1. In contrast,
LRP5 -deficient islets lacked the Wnt-3a-stimulated insulin
secretion. These data suggest that Wnt/ ***LRP5*** signaling
contributes to the glucose-induced insulin secretion in the islets.

L7 ANSWER 53 OF 68 MEDLINE on STN
DUPLICATE 22
ACCESSION NUMBER: 2003285530 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12812787
TITLE: A role for Wnt/beta-catenin signaling in lens epithelial
differentiation.
AUTHOR: Stump Richard J W; Ang Sharyn; Chen Yongjuan; von Bahr
Tatiana; Lovicu Frank J; Pinson Kathleen; de Iongh Robbert
U; Yamaguchi Terry P; Sassoon David A; McAvoy John W
CORPORATE SOURCE: Save Sight Institute, The University of Sydney, Sydney

Hospital & Eye Hospital, GPO Box 4337, NSW 2006, Australia.
CONTRACT NUMBER: R01 EYO3177 (NEI)
SOURCE: Developmental biology, (2003 Jul 1) 259 (1) 48-61.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030619
Last Updated on STN: 20030723
Entered Medline: 20030722
AB The differentiation of epithelial cells and fiber cells from the anterior
and posterior compartments of the lens vesicle, respectively, give the
mammalian lens its distinctive polarity. While much progress has been
made in understanding the molecular basis of fiber differentiation, little
is known about factors that govern the differentiation of the epithelium.
Members of the Wnt growth factor family appear to be key regulators of
epithelial differentiation in various organ systems. Wnts are ligands for
Frizzled receptors and can activate several signaling pathways, of which
the best understood is the Wnt/beta-catenin pathway. The presence of
LDL-related protein coreceptors (LRPs) 5 or 6 has been shown to be a
requirement for Wnt signaling through the beta-catenin pathway. To access
the role of this signaling pathway in the lens, we analyzed mice with a
null mutation of lrp6. These mice had small eyes and aberrant lenses,
characterized by an incompletely formed anterior epithelium resulting in
extrusion of the lens fibers into the overlying corneal stroma. We also
showed that multiple Wnts, including 5a, 5b, 7a, 7b, 8a, 8b, and Frizzled
receptors 1, 2, 3, 4, and 6, were detected in the lens. Expression of
these molecules was generally present throughout the lens epithelium and
extended into the transitional zone, where early fiber elongation occurs.
In addition to both ***LRP5*** and LRP6, we also showed the expression
of other molecules involved in Wnt signaling and its regulation, including
Dishevelleds, Dickkopfs, and secreted Frizzled-related proteins. Taken
together, these results indicate a role for Wnt signaling in regulating
the differentiation and behavior of lens cells.

L7 ANSWER 54 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:841503 CAPLUS
TITLE: Secreted antagonists/modulators of Wnt signaling
AUTHOR(S): Semenov, Mikhail V.; He, Xi
CORPORATE SOURCE: Division of Neuroscience, Department of Neurology,
Children's Hospital/Harvard Medical School, Boston,
MA, USA
SOURCE: Wnt Signaling in Development (2003), 15-34.
Editor(s): Kuehl, Michael. Landes Bioscience:
Georgetown, Tex.
CODEN: 69FYH5; ISBN: 0-306-47838-2
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Wnt signaling is controlled by a plethora of extracellular modulators that
bind either Wnt mols. or Wnt receptors. These modulators in most cases
function to antagonize Wnt signaling and in concept define the range,
amplitude, and duration of Wnt signaling. Four conserved but structurally
distinct families of Wnt antagonists are currently known from lower
vertebrates to human: sFRP (secreted frizzled related protein), WIF-1
(Wnt-inhibitory factor 1), Cerberus, and Dickkopf (Dkk). SFRP proteins,
WIF-1 and Cerberus have been shown to bind Wnt mols. and may inhibit
multiple signaling pathways activated by these Wnt mols. ***Dkk***
proteins bind to the Wnt co-receptor ***LRP5*** /LRP6, and
specifically inhibit (but in some cases stimulate) ***LRP5***
/LRP6-dependent Wnt/.beta.-catenin signaling. In Drosophila, secreted
Wingful/Notum antagonizes Wingless (Wnt) signaling by functioning as a
modifying enzyme for Dally and Dally-like, proteoglycans that may
facilitate the Wnt receptor interaction. Secreted Wnt antagonists play
crit. roles in embryogenesis and are implicated in variety of physiol. and
pathol. processes.
REFERENCE COUNT: 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 55 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2004233774 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12729465
TITLE: Wnt/Wingless signaling through beta-catenin requires the
function of both LRP/Arrow and frizzled classes of
receptors.
AUTHOR: Schweizer Liang; Varmus Harold
CORPORATE SOURCE: Cell Biology Program, Sloan-Kettering Institute for Cancer
Research, 1275 York Avenue, New York, NY 10021, USA..
schweizl@mskcc.org
SOURCE: BMC cell biology [electronic resource], (2003 May 2) 4 (1)
4.

Journal code: 100966972. ISSN: 1471-2121.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20040511
Last Updated on STN: 20050122
Entered Medline: 20050121
AB BACKGROUND: Wnt/Wingless (Wg) signals are transduced by seven-transmembrane Frizzleds (Fzs) and the single-transmembrane ***LDL*** - ***receptor*** - ***related*** ***proteins*** ***5*** or 6 (***LRP5*** /6) or Arrow. The aminotermini of LRP and Fz were reported to associate only in the presence of Wnt, implying that Wnt ligands form a trimeric complex with two different receptors. However, it was recently reported that LRPs activate the Wnt/beta-catenin pathway by binding to Axin in a Dishevelled--independent manner, while Fzs transduce Wnt signals through Dishevelled to stabilize beta-catenin. Thus, it is possible that ***Wnt*** ***proteins*** form separate complexes with Fzs and LRPs, transducing Wnt signals separately, but converging downstream in the Wnt/beta-catenin pathway. The question then arises whether both receptors are absolutely required to transduce Wnt signals. RESULTS: We have established a sensitive luciferase reporter assay in Drosophila S2 cells to determine the level of Wg--stimulated signaling. We demonstrate here that Wg can synergize with DFz2 and function cooperatively with LRP to activate the beta-catenin/Armadillo signaling pathway. Double-strand RNA interference that disrupts the synthesis of either receptor type dramatically impairs Wg signaling activity. Importantly, the pronounced synergistic effect of adding Wg and DFz2 is dependent on Arrow and Dishevelled. The synergy requires the cysteine-rich extracellular domain of DFz2, but not its carboxyterminus. Finally, mammalian LRP6 and its activated forms, which lack most of the extracellular domain of the protein, can activate the Wg signaling pathway and cooperate with Wg and DFz2 in S2 cells. We also show that the aminoterminus of LRP/Arr is required for the synergy between Wg and DFz2. CONCLUSION: Our study indicates that Wg signal transduction in S2 cells depends on the function of both LRPs and DFz2, and the results are consistent with the proposal that Wnt/Wg signals through the aminoterminal domains of its dual receptors, activating target genes through Dishevelled.

L7 ANSWER 56 OF 68 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:323467 BIOSIS
DOCUMENT NUMBER: PREV200300323467
TITLE: Wnt/Wingless signaling through beta-catenin requires the function of both LRP/Arrow and Frizzled classes of receptors.
AUTHOR(S): Schweizer, Liang [Reprint Author]; Varmus, Harold
CORPORATE SOURCE: Cell Biology Program, Sloan-Kettering Institute for Cancer Research, 1275 York Avenue, New York, NY, 10021, USA
schweizl@mskcc.org; varmus@mskcc.org
SOURCE: BMC Cell Biology, (May 2 2003) Vol. 4, No. 4 Cited June 13, 2003. http://www.biomedcentral.com/1471-2121. online.
ISSN: 1471-2121 (ISSN online).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jul 2003
Last Updated on STN: 9 Jul 2003
AB Background: Wnt/Wingless (Wg) signals are transduced by seven-transmembrane Frizzleds (Fzs) and the single-transmembrane LDL-receptor-3related proteins 5 or 6 (***LRP5*** /6) or Arrow. The aminotermini of LRP and Fz were reported to associate only in the presence of Wnt, implying that Wnt ligands form a trimeric complex with two different receptors. However, it was recently reported that LRPs activate the Wnt/beta-catenin pathway by binding to Axin in a Dishevelled - independent manner, while Fzs transduce Wnt signals through Dishevelled to stabilize beta-catenin. Thus, it is possible that ***Wnt*** ***proteins*** form separate complexes with Fzs and LRPs, transducing Wnt signals separately, but converging downstream in the Wnt/beta-catenin pathway. The question then arises whether both receptors are absolutely required to transduce Wnt signals. Results: We have established a sensitive luciferase reporter assay in Drosophila S2 cells to determine the level of Wg - stimulated signaling. We demonstrate here that Wg can synergize with DFz2 and function cooperatively with LRP to activate the beta-catenin/Armadillo signaling pathway. Double-strand RNA interference that disrupts the synthesis of either receptor type dramatically impairs Wg signaling activity. Importantly, the pronounced synergistic effect of adding Wg and DFz2 is dependent on Arrow and Dishevelled. The synergy

requires the cysteine-rich extracellular domain of DFz2, but not its carboxyterminus. Finally, mammalian LRP6 and its activated forms, which lack most of the extracellular domain of the protein, can activate the Wg signaling pathway and cooperate with Wg and DFz2 in S2 cells. We also show that the aminoterminus of LRP/Arr is required for the synergy between Wg and DFz2. Conclusion: Our study indicates that Wg signal transduction in S2 cells depends on the function of both LRPs and DFz2, and the results are consistent with the proposal that Wnt/Wg signals through the aminoterminal domains of its dual receptors, activating target genes through Dishevelled.

L7 ANSWER 57 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2002275003 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12015398
TITLE: Regulation of bone formation and vision by ***LRP5*** .
COMMENT: Comment on: N Engl J Med. 2002 May 16;346(20):1513-21.
PubMed ID: 12015390
AUTHOR: Patel Millan S; Karsenty Gerard
SOURCE: New England journal of medicine, (2002 May 16) 346 (20)
1572-4.
Journal code: 0255562. ISSN: 1533-4406.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Editorial
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Space
Life Sciences
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020517
Last Updated on STN: 20020623
Entered Medline: 20020522

L7 ANSWER 58 OF 68 MEDLINE on STN
DUPLICATE 23
ACCESSION NUMBER: 2002470888 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12121999
TITLE: A novel set of Wnt-Frizzled fusion proteins identifies
receptor components that activate beta -catenin-dependent
signaling.
AUTHOR: Holmen Sheri L; Salic Adrian; Zylstra Cassandra R;
Kirschner Marc W; Williams Bart O
CORPORATE SOURCE: Laboratory of Cell Signaling and Carcinogenesis, Van Andel
Research Institute, Grand Rapids, Michigan 49503, USA.
SOURCE: Journal of biological chemistry, (2002 Sep 20) 277 (38)
34727-35.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020917
Last Updated on STN: 20030105
Entered Medline: 20021024
AB ***Wnt*** ***proteins*** initiate the canonical (beta-catenin-regulated) signaling cascade by binding to seven-transmembrane spanning receptors of the Frizzled (Fz) family together with the coreceptors ***LRP5*** and -6, members of the low density lipoprotein receptor-related protein family (LRP). Several reports have shown physical and functional associations between various Wnt, LRP, and Frizzled molecules; however, the underlying mechanisms for selectivity remain poorly understood. We present data on a novel set of Wnt-Fz fusion constructs that are useful for elucidating mechanisms of Wnt signal transduction specificity in both Xenopus embryos and 293T cells. In 293T cells, coexpression of several Wnt-Fz fusion proteins with LRP6, but not ***LRP5*** , significantly activated a Wnt-responsive promoter, Optimized TOPFlash. Interestingly, ***Wnt*** ***proteins*** from both the Wnt1 and Wnt5A classes, when fused to the same Frizzled, can synergize with LRP6 to activate signaling and induce secondary axes in Xenopus embryos. However, when several Wnt-Fz constructs containing different Frizzled molecules were tested, it was found that all Frizzled molecules are not equivalent in their ability to activate the canonical Wnt pathway in this context. The data suggest that the distinction between the two Wnt classes lies not in intrinsic differences in the molecules but via the Frizzled molecules with which they interact.

L7 ANSWER 59 OF 68 MEDLINE on STN
DUPLICATE 24
ACCESSION NUMBER: 2002283362 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11884395
TITLE: Casein kinase I and casein kinase II differentially
regulate axin function in Wnt and JNK pathways.
AUTHOR: Zhang Yi; Qiu Wen-Jie; Chan Siu Chiu; Han Jiahuai; He Xi;
Lin Sheng-Cai
CORPORATE SOURCE: Department of Biochemistry, Hong Kong University of Science
and Technology, Clear Water Bay, Kowloon, Hong Kong, China.
SOURCE: Journal of biological chemistry, (2002 May 17) 277 (20)
17706-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020528
Last Updated on STN: 20030105
Entered Medline: 20020716
AB Axin uses different combinations of functional domains in down-regulation
of the Wnt pathway and activation of the MEKK1/JNK pathway. We are
interested in the elucidation of the functional switch of Axin. In the
present study, we show that the Wnt activator CKIepsilon, but not
CKIIalpha, Frat1, ***LRP5*** , or LRP6, inhibited Axin-mediated JNK
activation. We also found that both CKIalpha and CKIepsilon interacted
with Axin, whereas CKIIalpha did not bind to Axin and had no effect on
Axin-mediated JNK activity even though CKIIalpha has also been suggested
to be an activator for the Wnt pathway. The COOH-terminal region and the
MEKK1-interacting domain of Axin are important for CKIalpha-Axin and
CKIepsilon-Axin interaction. We further demonstrated that CKIepsilon and
CKIalpha binding to Axin excluded MEKK1 binding, indicating that a
competitive physical occupancy may underlie the inhibitory effect.
Moreover, our data indicated that CKIepsilon kinase activity plays an
additive role in this effect. Taken together, we have demonstrated that
CKI and CKII exhibit differential effects on Axin-MEKK1 interaction and
Axin-mediated JNK activation. Furthermore, our data suggest that CKI may
provide a possible switch mechanism for Axin function in the regulation of
Wnt and JNK pathways.

L7 ANSWER 60 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 25
ACCESSION NUMBER: 2002:360588 CAPLUS
DOCUMENT NUMBER: 137:291952
TITLE: Regulation of bone formation and vision by
LRP5
AUTHOR(S): Patel, Millan S.; Karsenty, Gerard
CORPORATE SOURCE: Baylor College Med., Houston, TX, 77030, USA
SOURCE: New England Journal of Medicine (2002), 346(20),
1572-1574
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review on the lock-and-key mechanism involving low d. lipoprotein
receptor-related protein 5 (***LRP5***) that regulates bone formation
and vision. Carriers of ***LRP5*** loss-of-function mutations have a
lower bone mass than noncarriers, suggesting that the effects of this gene
are dominant for the regulation of bone mass. Secreted proteins from the
Dickkopf family bind with high affinity to ***LRP5*** or its closely
related homolog, LRP6, and thus directly prevent binding of ***Wnt***
proteins .
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 61 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2002274995 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12015390
TITLE: High bone density due to a mutation in ***LDL*** -
receptor - ***related*** ***protein***
5 .
COMMENT: Comment in: N Engl J Med. 2002 May 16;346(20):1572-4.
PubMed ID: 12015398
Comment in: N Engl J Med. 2002 Sep 19;347(12):943-4; author
reply 943-4. PubMed ID: 12239268
Comment in: N Engl J Med. 2002 Sep 19;347(12):943-4; author
reply 943-4. PubMed ID: 12240686
Comment in: N Engl J Med. 2004 May 13;350(20):2096-9;
author reply 2096-9. PubMed ID: 15141052
AUTHOR: Boyden Lynn M; Mao Junhao; Belsky Joseph; Mitzner Lyle;
Farhi Anita; Mitnick Mary A; Wu Dianqing; Insogna Karl;
Lifton Richard P
CORPORATE SOURCE: Department of Genetics, Yale University School of Medicine,
New Haven, Connecticut 06510, USA.
CONTRACT NUMBER: AG15345 (NIA)
AR46032 (NIAMS)
CA85420 (NCI)
RR00125 (NCRR)
SOURCE: New England journal of medicine, (2002 May 16) 346 (20)
1513-21.
Journal code: 0255562. ISSN: 1533-4406.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020517
Last Updated on STN: 20020926
Entered Medline: 20020522
AB BACKGROUND: Osteoporosis is a major public health problem of largely
unknown cause. Loss-of-function mutations in the gene for low-density
lipoprotein receptor-related protein 5 (***LRP5***), which acts in the
Wnt signaling pathway, have been shown to cause osteoporosis-pseudoglioma.
METHODS: We performed genetic and biochemical analyses of a kindred with

an autosomal dominant syndrome characterized by high bone density, a wide
and deep mandible, and torus palatinus. RESULTS: Genetic analysis
revealed linkage of the syndrome to chromosome 11q12-13 (odds of linkage,
>1 million to 1), an interval that contains ***LRP5*** . Affected
members of the kindred had a mutation in this gene, with valine
substituted for glycine at codon 171 (LRP5V171). This mutation segregated
with the trait in the family and was absent in control subjects. The
normal glycine lies in a so-called propeller motif that is highly
conserved from fruit flies to humans. Markers of bone resorption were
normal in the affected subjects, whereas markers of bone formation such as
osteocalcin were markedly elevated. Levels of fibronectin, a known target
of signaling by Wnt, a developmental protein, were also elevated. In
vitro studies showed that the normal inhibition of Wnt signaling by
another protein, Dickkopf-1 (Dkk-1), was defective in the presence of
LRP5V171 and that this resulted in increased signaling due to unopposed
Wnt activity. CONCLUSIONS: The LRP5V171 mutation causes high bone
density, with a thickened mandible and torus palatinus, by impairing the
action of a normal antagonist of the Wnt pathway and thus increasing Wnt
signaling. These findings demonstrate the role of altered ***LRP5***
function in high bone mass and point to Dkk as a potential target for the
prevention or treatment of osteoporosis.

L7 ANSWER 62 OF 68 MEDLINE on STN
DUPLICATE 26
ACCESSION NUMBER: 2002308401 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12050670
TITLE: Kremen proteins are Dickkopf receptors that regulate
Wnt/beta-catenin signalling.
AUTHOR: Mao Bingyu; Wu Wei; Davidson Gary; Marhold Joachim; Li
Mingfa; Mechler Bernard M; Delius Hajo; Hoppe Dana; Stannek
Peter; Walter Carmen; Glinka Andrei; Niehrs Christof
CORPORATE SOURCE: Molecular Embryology Division, Deutsches
Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120
Heidelberg, Germany.
SOURCE: Nature, (2002 Jun 6) 417 (6889) 664-7.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ457192
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020611
Last Updated on STN: 20020703
Entered Medline: 20020702
AB The Wnt family of secreted glycoproteins mediate cell cell interactions
during cell growth and differentiation in both embryos and adults.
Canonical Wnt signalling by way of the beta-catenin pathway is transduced
by two receptor families. Frizzled proteins and lipoprotein-receptor-
related proteins 5 and 6 (***LRP5*** /6) bind Wnts and transmit their
signal by stabilizing intracellular beta-catenin. Wnt/beta-catenin
signalling is inhibited by the secreted protein Dickkopf1 (Dkk1), a member
of a multigene family, which induces head formation in amphibian embryos.
Dkk1 has been shown to inhibit Wnt signalling by binding to and
antagonizing ***LRP5*** /6. Here we show that the transmembrane
proteins Kremen1 and Kremen2 are high-affinity Dkk1 receptors that
functionally cooperate with Dkk1 to block Wnt/beta-catenin signalling.
Kremen2 forms a ternary complex with Dkk1 and LRP6, and induces rapid
endocytosis and removal of the Wnt receptor LRP6 from the plasma membrane.
The results indicate that Kremen1 and Kremen2 are components of a membrane
complex modulating canonical Wnt signalling through LRP6 in vertebrates.

L7 ANSWER 63 OF 68 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2002346039 EMBASE
TITLE: The gene for high bone mass.
AUTHOR: Johnson M.L.; Picconi J.L.; Recker R.R.
CORPORATE SOURCE: Dr. M.L. Johnson, Osteoporosis Research Center, Creighton
Univ. School of Medicine, 601 North 30th Street, Omaha, NE
68131, United States.
MARKL@creighton.edu
SOURCE: Endocrinologist, (2002) 12/5 (445-453).
Refs: 79
ISSN: 1051-2144 CODEN: EDOCEB
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The mass, density, and architecture of the skeleton are adapted to enable
it to perform its mechanical, protective, and metabolic functions.
Osteoporosis is a condition of lost adaptation characterized by decreased
skeletal mass and density and increased skeletal fragility. Many diseases
result in increased bone density, including osteopetrosis and Paget's

disease, but deformities or bony lesions with decreased skeletal integrity
usually accompany these conditions. We have identified a kindred with high
bone mass (HBM) yet normally shaped bones. Linkage analysis localized the
gene for the HBM trait to chromosome 11 (11q12-13). Subsequent physical
mapping and mutation analysis have identified the cause as a point
mutation in the ***LDL*** ***receptor*** - ***related***
protein ***5*** (***Lrp5***) gene that results in a valine
substitution for glycine at position 171 in the protein. This protein is
important in the Wnt signaling pathway. The authors have hypothesized that
the ***Lrp5*** gene/pathway is part of the mechanism by which bone
senses mechanical load. Increased bone strength, HBM, and a phenotype
resembling our human kindred develop in transgenic mice carrying the human
Lrp5 gene with the HBM mutation. Recent data indicate that the HBM
mutation reduces the threshold for response of the skeleton to mechanical
load resulting in an overadaptation to normal mechanical loads. This
discovery has opened the door to understanding one of the most important
paradigms in bone biology, how bones respond and adapt to mechanical
loading. Understanding the mechanosensation pathway and its regulation
will lead us to new treatments for osteoporosis.

L7 ANSWER 64 OF 68 MEDLINE on STN
DUPLICATE 27
ACCESSION NUMBER: 2002448371 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12204281
TITLE: Cloning and expression of Xenopus ***Lrp5*** and Lrp6
genes.
AUTHOR: Houston Douglas W; Wylie Chris
CORPORATE SOURCE: Division of Developmental Biology, Cincinnati Children's
Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH
45229-3039, USA.
CONTRACT NUMBER: F32 HD40716-01 (NICHD)
SOURCE: Mechanisms of development, (2002 Sep) 117 (1-2) 337-42.
Journal code: 9101218. ISSN: 0925-4773.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF276084; GENBANK-BG017115
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20020904
Last Updated on STN: 20030410
Entered Medline: 20030409
AB ***LRP5*** and LRP6 comprise a subfamily of lipoprotein-receptor
related proteins that function as co-receptors for ***Wnt***
proteins . Mutation of human ***LRP5*** is responsible for
osteoporosis-pseudoglioma syndrome and disruption of Lrp6 in mice causes
similar effects to mutation of several different Wnt genes. We have
cloned Xenopus homologues of ***Lrp5*** and Lrp6 (Xlrp5, Xlrp6) and
examined their expression during embryogenesis. Both genes are expressed
maternally and ubiquitously through early development. At later stages,
Xlrp5 is found in the eye, forebrain, hindbrain, branchial arches and the
tip of the tail bud. Xlrp6 is expressed throughout the central nervous
system, branchial arches, in the eye and otic vesicle. Both genes are
also expressed at the intersomitic boundary. These results suggest roles
for Wnt signaling via LRP proteins in these tissues.

L7 ANSWER 65 OF 68 MEDLINE on STN
DUPLICATE 28
ACCESSION NUMBER: 2002219603 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11956231
TITLE: Cbfa1-independent decrease in osteoblast proliferation,
osteopenia, and persistent embryonic eye vascularization in
mice deficient in ***Lrp5*** , a Wnt coreceptor.
AUTHOR: Kato Masaki; Patel Millan S; Levasseur Regis; Lobov Ivan;
Chang Benny H-J; Glass Donald A 2nd; Hartmann Christine; Li
Lan; Hwang Tae-Ho; Brayton Cory F; Lang Richard A; Karsenty
Gerard; Chan Lawrence
CORPORATE SOURCE: Department of Molecular and Cellular Biology and Medicine,
Baylor College of Medicine, Houston, TX 77030, USA.
CONTRACT NUMBER: AR42919 (NIAMS)
DE11290 (NIDCR)
DK58882 (NIDDK)
HL16512 (NHLBI)
HL51586 (NHLBI)
SOURCE: Journal of cell biology, (2002 Apr 15) 157 (2) 303-14.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020417
Last Updated on STN: 20030105
Entered Medline: 20020516
AB The low-density lipoprotein receptor-related protein (Lrp)-5 functions as
a Wnt coreceptor. Here we show that mice with a targeted disruption of
Lrp5 develop a low bone mass phenotype. In vivo and in vitro
analyses indicate that this phenotype becomes evident postnatally, and

demonstrate that it is secondary to decreased osteoblast proliferation and
function in a Cbfa1-independent manner. ***Lrp5*** is expressed in
osteoblasts and is required for optimal Wnt signaling in osteoblasts. In
addition, ***Lrp5*** -deficient mice display persistent embryonic eye
vascularization due to a failure of macrophage-induced endothelial cell
apoptosis. These results implicate ***Wnt*** ***proteins*** in
the postnatal control of vascular regression and bone formation, two
functions affected in many diseases. Moreover, these features
recapitulate human osteoporosis-pseudoglioma syndrome, caused by
LRP5 inactivation.

L7 ANSWER 66 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2001471554 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11516963
TITLE: Wnt signalling: antagonistic Dickkopfs.
COMMENT: Comment on: Curr Biol. 2000 Dec 14-28;10(24):1611-4. PubMed
ID: 11137016
Comment on: Curr Biol. 2001 Jun 26;11(12):951-61. PubMed
ID: 11448771
AUTHOR: Zorn A M
CORPORATE SOURCE: Wellcome/CRC Institute of Cancer and Developmental Biology,
Tennis Court Road, Cambridge CB2 1QR, UK.
SOURCE: Current biology : CB, (2001 Aug 7) 11 (15) R592-5.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010823
Last Updated on STN: 20020424
Entered Medline: 20011204
AB Dickkopf proteins are secreted antagonists of the Wnt cell signalling
molecules, which have a novel mode of action. Dickkopf1 binds to the
LRP5 /6 Wnt co-receptor and prevents the formation of active
Wnt--Frizzled-- ***LRP5*** /6 receptor complexes, thus blocking the
canonical Wnt--beta-catenin pathway.

L7 ANSWER 67 OF 68 MEDLINE on STN
DUPLICATE 29
ACCESSION NUMBER: 2001673198 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11719191
TITLE: ***LDL*** ***receptor*** - ***related***
protein ***5*** (***LRP5***) affects bone
accrual and eye development.
AUTHOR: Gong Y; Slee R B; Fukai N; Rawadi G; Roman-Roman S;
Reginato A M; Wang H; Cundy T; Glorieux F H; Lev D;
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Journal code: 0413066. ISSN: 0092-8674.
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DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
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AB In humans, low peak bone mass is a significant risk factor for
osteoporosis. We report that ***LRP5*** , encoding the low-density
lipoprotein receptor-related protein 5, affects bone mass accrual during
growth. Mutations in ***LRP5*** cause the autosomal recessive
disorder osteoporosis-pseudoglioma syndrome (OPPG). We find that OPPG
carriers have reduced bone mass when compared to age- and gender-matched
controls. We demonstrate ***LRP5*** expression by osteoblasts in situ
and show that ***LRP5*** can transduce Wnt signaling in vitro via the
canonical pathway. We further show that a mutant-secreted form of
LRP5 can reduce bone thickness in mouse calvarial explant
cultures. These data indicate that Wnt-mediated signaling via
LRP5 affects bone accrual during growth and is important for the
establishment of peak bone mass.

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ACCESSION NUMBER: 2000477637 MEDLINE
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TITLE: LDL-receptor-related proteins in Wnt signal transduction.
AUTHOR: Tamai K; Semenov M; Kato Y; Spokony R; Liu C; Katsuyama Y;
Hess F; Saint-Jeannet J P; He X

CORPORATE SOURCE: Division of Neuroscience, Children's Hospital, Harvard
Medical School, Boston, Massachusetts 02115, USA.
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AB The Wnt family of secreted signalling molecules are essential in embryo development and tumour formation. The Frizzled (Fz) family of serpentine receptors function as Wnt receptors, but how Fz proteins transduce signalling is not understood. In Drosophila, arrow phenocopies the wingless (DWnt-1) phenotype, and encodes a transmembrane protein that is homologous to two members of the mammalian low-density lipoprotein receptor (LDLR)-related protein (LRP) family, ***LRP5*** and LRP6 (refs 12-15). Here we report that LRP6 functions as a co-receptor for Wnt signal transduction. In Xenopus embryos, LRP6 activated Wnt-Fz signalling, and induced Wnt responsive genes, dorsal axis duplication and neural crest formation. An LRP6 mutant lacking the carboxyl intracellular domain blocked signalling by Wnt or Wnt-Fz, but not by Dishevelled or beta-catenin, and inhibited neural crest development. The extracellular domain of LRP6 bound Wnt-1 and associated with Fz in a Wnt-dependent manner. Our results indicate that LRP6 may be a component of the Wnt receptor complex.

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